

Review Article

Left bundle branch pacing: Case-based discussion of concept and criteria

ABSTRACT

Cardiac pacing is the mainstay of therapy for symptomatic bradyarrhythmias due to conduction system disease. However, traditional right ventricular apical or septal pacing results in dyssynchronous activation of the left ventricle and pacing-related cardiomyopathy in a subset of patients. Conduction system pacing, by directly capturing elements of the cardiac conduction system aims to produce physiologic activation of the ventricles. His bundle pacing, while being the most physiologic way of achieving this, suffers from certain limitations. Left bundle branch (LBB) pacing has emerged in recent times as a promising alternative modality of conduction system pacing. In this review, we outline the concept and criteria for successful LBB pacing through illustrative cases.

Keywords: Conduction system pacing, criteria, left bundle branch pacing, physiological pacing

INTRODUCTION

Cardiac pacing is the only effective therapy for symptomatic bradycardia in the absence of reversible causes. Right ventricular (RV) apical pacing has been in widespread use for >50 years but causes electrical and mechanical dyssynchrony in the ventricles, with an attendant increased long-term risk for heart failure and atrial fibrillation.^[1,2] Pacing at alternative RV sites, such as the septum or outflow tract, has not been shown to be superior to RV apical pacing.^[3,4]

This has led to renewed interest in physiological pacing by recruiting the conduction system. His bundle pacing (HBP), by screwing an active fixation lead at the His bundle location to capture the His [Figure 1a] was first successfully achieved by Deshmukh *et al.*, and published more than two decades back.^[6] Despite being the most physiological modality of ventricular pacing, HBP has some limitations. HBP has a narrow target range and identifying the precise location can be challenging. Owing to the location of the His bundle at the Tricuspid annulus, low R-wave amplitude, and large atrial signals can be encountered, resulting in ventricular undersensing and atrial oversensing. A late rise in the pacing threshold has been described in 5%–10% of patients.

Damage to the His bundle during implantation and risk of lead dislodgement are other potential concerns. Finally, although even bundle branch blocks are often intra-Hisian and corrected in many instances by HBP owing to longitudinal dissociation of fibers within the His, true infra-Hisian conduction system block cannot be overcome by HBP.^[7-11]

Left bundle branch pacing (LBBP) can potentially solve many of the limitations associated with HBP. LBBP was first described by Huang *et al.*, in which the pacing lead is penetrated deep into the inter-ventricular septum (IVS) to place it subendocardially in the left ventricle (LV) at the location of the left bundle branch (LBB). By directly capturing the LBB fibers, it achieves synchronous LV activation and

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physiological pacing [Figure 1b]. As the lead location is completely ventricular, deep in the IVS, LBBP is characterized by a stable lead position, lower risk of dislodgement, a low and stable pacing threshold, ability to overcome truly infra Hisian block and a relative technical ease of implantation due to a wider target, as the broad LBB occupies a wider area compared to the narrow His bundle. Hence in recent times, LBBP has increasingly become the more preferred mode of conduction system pacing.^[12]

In this paper, we illustrate the concept of LBBP and elucidate the criteria for satisfactory LBB capture through a case-based approach.

CASE REPORTS

Case 1

A 63-year-old female, a known case of systemic hypertension, type 2 diabetes mellitus (DM), and hypothyroidism presented with exertional fatigue and shortness of breath. She had bradycardia at presentation with a pulse rate of 40/min. A 12 lead electrocardiogram (ECG) showed 2:1 atrioventricular (AV) block, right bundle branch block (RBBB), rate of 44/min [Figure 2a]. Her baseline blood parameters were normal. A coronary angiogram showed normal epicardial coronaries. Dual chamber permanent pacemaker implantation with LBB pacing was planned in view of the symptomatic 2:1 AV block. Echocardiogram showed normal LV systolic function with basal IVS thickness (1.5 cm distal to AV leaflet attachment) of 12 mm. Knowing IVS thickness at the site of LBB lead placement is important to ascertain the depth of safe penetration and avoid perforation into the LV cavity. The distance from the tip of the helix to the anode is 10.8 mm in the Medtronic SelectSecure 3830 lead.

Procedure steps

A temporary pacing lead was placed in RV apex and a quadripolar electrophysiology catheter was placed at His location via the right femoral vein route to serve as a landmark to guide left bundle lead placement. A standard left infraclavicular subcutaneous pacemaker pocket was created and two left axillary venous accesses were taken. A Medtronic Select-Secure lumenless 3830 69 cm long lead was introduced via a Medtronic C315 His preshaped long sheath (Medtronic Inc., CA, USA). Alligator clips were attached to the lead and skin to display intracardiac signals and pace from the lead tip in unipolar mode. The preshaped sheath has a primary and secondary (septal) curve, which helps to reach the point of interest in the IVS. The sheath was advanced into the RV in the right anterior oblique 30° view and then further along an imaginary line connecting the His catheter to the RV apex to a spot about 1.5–2 cm distal to the His location [Figure 3a and b].

Contact was achieved on the IVS with the distal tip of the lead extended just beyond the sheath. Pacing through the lead tip was done and its position was fine-tuned to obtain a paced QRS morphology showing a notched QRS (W pattern) in V1, R wave in lead II, rS wave in lead III, and discordant QRS in aVR (negative) and aVL (positive). Obtaining this QRS morphology indicates that the lead is in the right position to capture the LBB after penetrating the IVS. The initial impedance reading before lead penetration was noted. Changing to left anterior

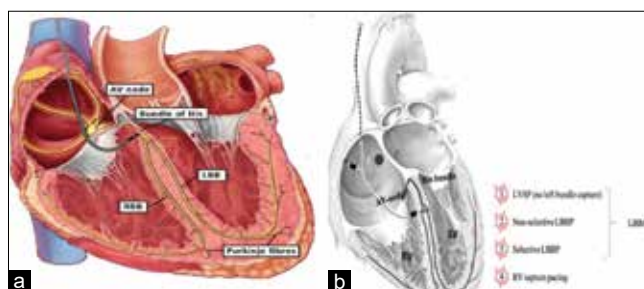


Figure 1: (a) Illustration of His bundle pacing, (b) Schematic overview of heart and conduction system illustrating where the lead penetrates interventricular septum to achieve left bundle branch pacing. AV: Atrioventricular, LVSP: Left ventricular septal pacing, LBB: Left bundle branch, LBBP: LBB pacing, RBB: Right bundle branch, LBBAP: left bundle branch area pacing, LV: Left ventricle, RV: Right ventricle (Reproduced from Heckman et al.^[5])

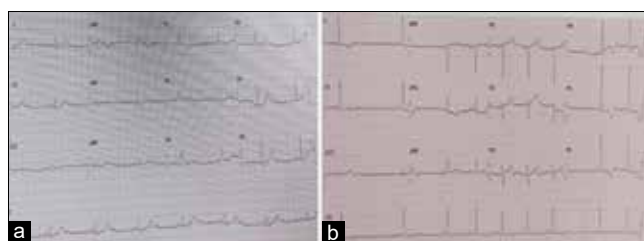


Figure 2: (a) Electrocardiogram (ECG) showing 2:1 atrioventricular block with right bundle branch block in Case 1, (b) ECG showing sinus node dysfunction in Case 2

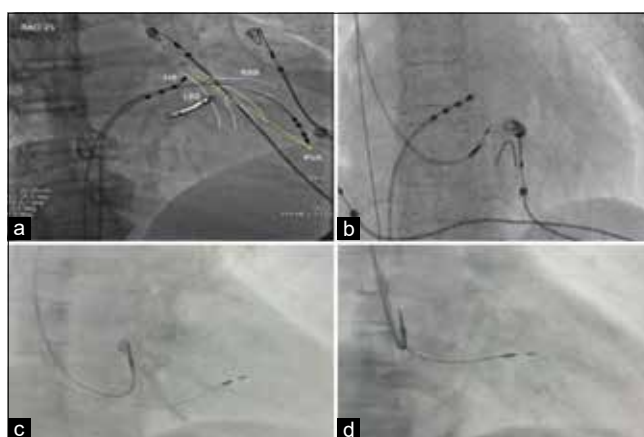


Figure 3: (a and b) Fluoroscopic views in the right anterior oblique showing the site of the left bundle branch pacing lead implantation (Reproduced from Ponnusamy et al.^[13]) (c and d) Final fluoroscopic images of Case 1 and Case 2, respectively. RAO: Right anterior oblique, RBB: Right bundle branch, LBB: Left bundle branch, RVA: ???

oblique 30° view, the sheath was rotated counterclockwise to orient it perpendicular to the IVS and provide good support for lead penetration. Five to six rapid turns were then given to the lead to penetrate the IVS. Ventricular ectopics, if any, generated during lead penetration (fixation beats) were documented. An initial increase in impedance followed by a drop and a good current of injury were used as indicators of adequate lead penetration. Sufficient R wave amplitude, low pacing threshold and LBB capture were checked and gradual additional turns were given as needed to achieve LBB capture with good parameters. The impedance and current of injury in the ventricular electrogram are carefully monitored while penetrating the IVS with the lead. An excessive fall in impedance (to <500 Ω) or loss of injury current indicates perforation into the LV cavity. In that case, the lead has to be completely removed and re-positioned in a fresh location. Once the lead had adequately penetrated and LBB capture confirmed, the sheath was slit and parameters rechecked. The final unipolar pacing impedance was >500 Ω.

This was followed by the fixation of the atrial lead in RA appendage, confirming lead parameters and fixing both leads to the pulse generator.

Intra-procedure criteria for left bundle capture

Criteria used to determine LBB capture are listed in Table 1 and Figure 4. These include both ECG-based and intracardiac electrogram-based criteria. First, lead V1 should show a qR, Qr, or rsR' pattern. As the left bundle is being captured, it follows that V1 would show a RBBB-like morphology. The R wave peak time measured from the pacing spike to the peak of the R wave in lateral precordial leads (V5 and V6; also called peak LV activation time) should be short (<80 ms) and fixed at both high and low pacing outputs, showing that the lead is placed exactly at the LBB, leading to early

activation of LV lateral wall. The presence of an LBB potential recorded from the pacing lead tip can be considered the gold standard for ideal lead location; this is a sharp potential 15–30 ms before QRS. Demonstration of transition from nonselective to selective left bundle capture (with isoelectric interval between pacing pike and QRS) as the pacing output is reduced also serves to confirm that the lead is placed exactly at the LBB location. Ideally, all the above criteria should be demonstrated to confirm LBB capture specifically rather than mere LV septal myocardial capture, close to the LBB. These criteria are checked in unipolar pacing mode to have a pure representation of information from the pacing lead tip only. However, it is noteworthy that in finally pacing through the permanent pacemaker, bipolar, AV synchronous pacing is typically employed. This often gives rise to a narrow QRS without a classical RBBB pattern due to some myocardial capture from the anode on the RV septal side as well as varying degrees of fusion with intrinsic right bundle activation depending on the AV delay. Hence, the postprocedure ECGs may not reveal the same QRS pattern as obtained during intra-procedural testing [Figure 5a and b].

The final sensed R wave at implantation was 10.2 mV and the threshold was 1.1 V. The postprocedure fluoroscopic image is

Table 1: Parameters assessed to ascertain left bundle branch capture [Figures 4 and 7]

	Case 1	Case 2
rSR' pattern in V1	+	+
Narrow and fixed paced V6 RWPT (ms)	At 5 V: 61 At 1.5 V: 62	At 5 V: 77 At 1.5 V: 79
Left bundle potential	+	+
Nonselective to selective LBB capture transition at higher output to lower output	+	+
V6-V1 interpeak interval (ms)	37	33

LBB: Left bundle branch, V6RWPT: V6-R wave peak time

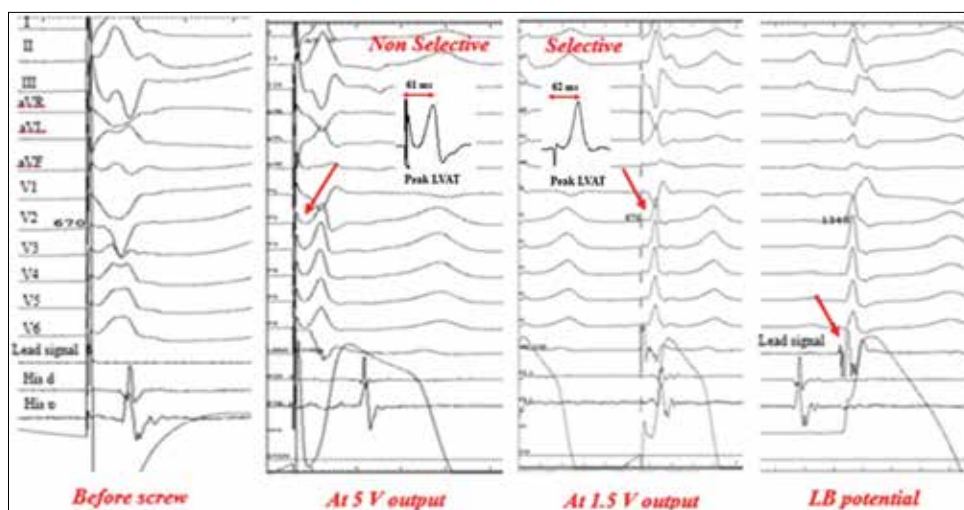


Figure 4: Electrograms during the left bundle branch capture in Case 1. LVAT: Left ventricular activation time

shown in Figure 3c. Postprocedure ECG showed atrial sensing with ventricular pacing with a narrow QRS duration of 80 ms due to recruitment of the left bundle [Figure 5a]. Lead positions in postprocedure chest X-ray are depicted in Figure 6a.

Case 2

A 76-year-old female, a known case of type II DM, systemic hypertension and coronary artery disease postrevascularisation to the left anterior descending in 2019 presented with exertional fatigue. ECG showed intermittent sinus bradycardia, atrial ectopics, and sinus pauses up to 1.8 s [Figure 2b]. Holter study showed sinus bradycardia with the lowest daytime heart rate of 39 bpm; brief atrial runs and pauses of up to 2.2 s suggestive of sick sinus syndrome. The echocardiogram was normal with a basal IVS thickness of 11.5 mm (1.5 cm distal to AV leaflet attachment).

Procedure steps

Similar procedural steps were followed as for Case 1 and successful LBB capture was obtained [Figure 7 and Table 1]. The final R wave amplitude at implantation was 18.0 mV and the threshold was 1.5 V. The postprocedure ECG showed atrial pacing with ventricular sensing. Postprocedure fluoroscopic image, ECG, and chest X-ray are depicted in Figures 3d, 5b, and 6b, respectively.

DISCUSSION

LBB pacing is increasingly being used as the preferred mode of conduction system pacing in view of its advantages over HBP. The learning curve for LBB pacing is also likely to be lesser compared to HBP. Various criteria have been put forward to ensure LBB capture during lead implantation.^[14] The paced QRS morphology, during unipolar LBBP, shows the pattern of RBBB in V1 lead or improving the LBB conduction in patients with LBB block (LBBB).^[15,16] The RBBB pattern is usually incomplete and is influenced by the level of capture of the distal His bundle or proximal left bundle, distal conduction system disease, and septal-Purkinje connections.

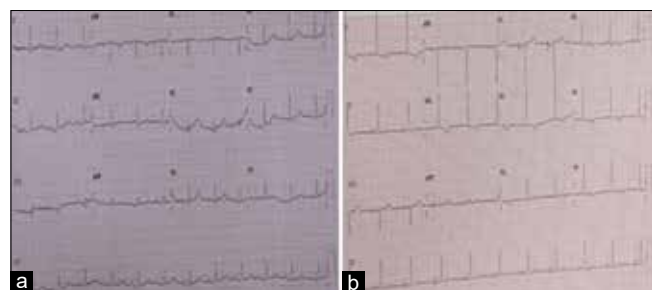


Figure 5: (a) Post left bundle branch (LBB) pacing electrocardiogram (ECG) showing A sensing, V pacing, PR interval 200 ms, QRS rate 72/min, and QRS duration 80 ms (Case 1), (b) Post-LBB pacing ECG showing A pacing, V sensing, PR interval 180 ms, QRS rate 60/min (Case 2)

With capture of the LBB during LBBP, we may demonstrate the LBB potential about 15–30 ms earlier to QRS.^[17,18] The interval from the LBB potential to V6-R wave peak time (V6RWPT) in intrinsic rhythm should be equal to the interval from stimulus to V6RWPT during pacing. Allowing for variability in measurement, a difference <10 ms has a sensitivity of 88.2% and specificity of 95.4% for confirming LBB capture.^[19]

The paced R wave peak time (RWPT) is measured from the onset of the pacing spike to the peak of the R wave in leads V5 and V6.^[12] It is an indicator of the rapidity of LV-free wall activation, useful to identify the depth of the pacing lead and capture of the LBB. On LBB capture, paced RWPT remains short and fixed at both high and low outputs. In patients with narrow QRS or isolated RBBB, V6RWPT <74 ms was 100% specific (albeit only 40% sensitive) for LBB capture, while a cutoff of ≤ 80 ms was 100% specific in patients with LBBB, nonspecific intraventricular conduction delay, and wide QRS escape rhythm.^[19] For practical purposes, cutoffs of <75 and <80 ms may be used, respectively.^[20]

During implantation, the pacing amplitude is slowly decreased to demonstrate a transition between simultaneous capture of both LBB and septal myocardium (nonselective-LBBP) to selective capture of either only LBB (s-LBBP) or only LV septal myocardium. Only 26.4% of patients with LBB/fascicular capture showed this feature in the MELOS registry,^[21] but the demonstration of s-LBBP has been reported in up to 75.4% of patients at implantation (and 30.9% at follow-up) when targeting more proximal LBBP sites.^[22]

The novel V6–V1 interpeak interval criterion uses a patient-specific reference (V1 R-wave peak and reflecting RV activation) to assess LV activation and is less impacted by conduction system disease than V6RWPT. The optimal cutoff is >33 ms,^[23] with a sensitivity of 71.8% and specificity of 90.0% for LBB capture, whereas >44 ms was 100% specific.^[24]

All the above-mentioned criteria were duly satisfied by the two cases discussed here.

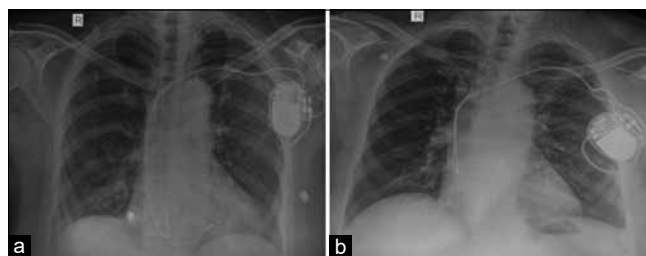


Figure 6: (a) Post left bundle branch (LBB) pacing Chest X-ray (Case 1), (b) Post LBB pacing Chest X-ray (Case 2)

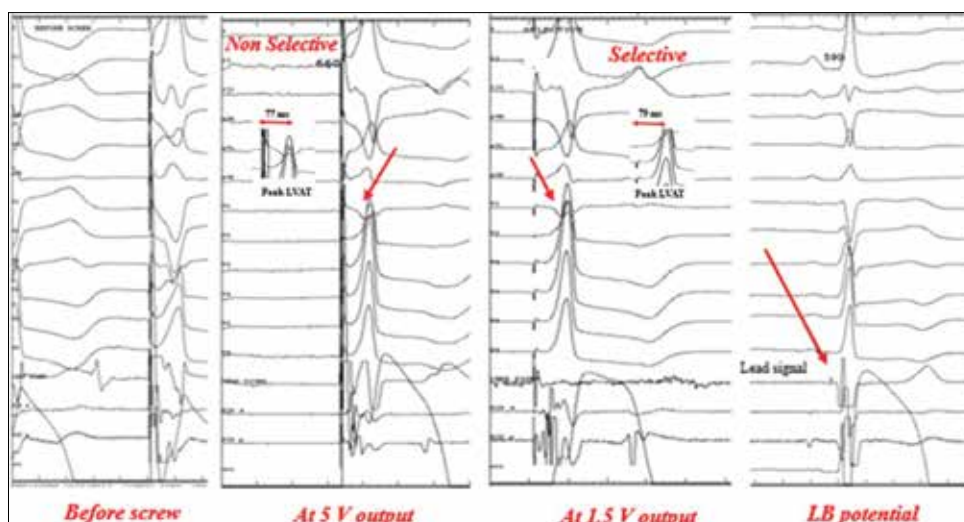


Figure 7: Electrograms during left bundle branch capture in Case 2. LVAT: Left ventricular activation time

In view of the ability to efficiently capture the LBB, giving rise to narrow QRS and early LV free wall activation, LBB pacing is being actively investigated as an alternative to cardiac resynchronization therapy (CRT) with promising results.^[25,26] Remaining knowledge gaps with regard to LBBP include a lack of long-term data, concerns about lead fracture at the hinge point where the lead penetrates the IVS as well as future lead extraction if needed, as the lead is buried deep in the IVS. Ongoing studies and registries with LBBP will give greater clarity on these issues.

CONCLUSION

LBB pacing is a rapidly evolving mode of conduction system pacing. With increase in experience, the criteria for LBB capture are getting further refined. It preserves all the advantages of conduction system recruitment, obtaining physiologic pacing, while overcoming some of the limitations of traditional HBP. A stepwise approach and meticulous assessment of proposed LBB capture criteria during implantation are needed to ensure success. With its role in bradycardia pacing as well as resynchronization therapy in heart failure patients, LBB pacing has the ability to transform the pacing landscape in the near future.

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Conflicts of interest

There are no conflicts of interest.

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Right coronary artery anatomy: Chronic total occlusion interventionist's perspective

ABSTRACT

Chronic total occlusion (CTO) intervention success has been improving with the evolution of newer devices and increasing operator expertise. In the recanalization of CTO, apart from CTO anatomy, occluded artery anatomy on either side of the CTO and collateral anatomy play a significant role in planning interventional strategy. Occluded artery anatomy affects the support provided by the guide for antegrade wiring, retrograde gear reach to the distal cap, selection of the site, and the type of reverse controlled antegrade and retrograde tracking and externalization. The right coronary artery (RCA) is the most common host for CTOs and shows many more variations in the course than other coronaries, posing specific challenges to interventionists while planning wiring strategies. The collateral entry pattern into RCA affects the retrograde gear reachability to the distal cap, steerability of wire, and support provided to retrograde wire escalation. Overall, some unique challenges interventionists face while treating RCA CTOs are linked to frequent anatomical variations in the origin from the aorta, tortuosity in the atrioventricular groove course, site of patent ductus arteriosus origin, and collateralization pattern both ipsilateral and contralateral. This manuscript describes anatomical variations of RCA and its collaterals, which interventionists should be mindful of while planning the wiring strategy and other procedural steps.

Keywords: Antegrade, chronic total occlusion, patent ductus arteriosus, retrograde, right coronary artery, tortuosity

INTRODUCTION

The last two decades have witnessed considerable progress in techniques and technologies that have increased the success rate of chronic total occlusion (CTO) interventions. In the recanalization of CTO, apart from CTO anatomy, occluded artery anatomy and collateral anatomy play significant roles in planning the interventional strategy.^[1] Occluded artery anatomy affects the support given for antegrade wiring, retrograde gear reach to the distal cap, site, and the type of reverse controlled antegrade and retrograde tracking (CART) and externalization. Anatomically, the right coronary artery (RCA) is not only the common host for CTOs^[2,3] but also shows much more course variations than other coronaries, posing challenges to interventionists while planning wiring strategies.^[2] Collateral entry into RCA affects the retrograde gear reachability to the distal cap, steerability of the wire, and support provided for retrograde wire escalation. The unique challenges interventionists face while opening RCA CTOs are

due to the frequent anatomical variations in the origin from the aorta, course in the atrioventricular (AV) groove, site of patent ductus arteriosus (PDA) origin, and collateralization pattern both ipsilateral and contralateral. This manuscript

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describes anatomical variations of RCA and its collaterals, which interventionists should be mindful of while planning wiring strategy and other procedural steps.

RIGHT CORONARY ARTERY ORIGIN AND PROXIMAL COURSE VARIATIONS

The anomalous origin of RCA is the most common among all coronary anomalies.^[4] The origin of RCA affects the choice of the guide catheter and the support given for antegrade wiring.^[4] Common RCA origin anomalies are anterior origin from the right sinus [Figure 1a], high anterior origin, and shepherd crook origin.^[5]

RIGHT CORONARY ARTERY ORIGIN IMPACT ON STUMPLESS OSTIAL RIGHT CORONARY ARTERY CHRONIC TOTAL OCCLUSION ASSESSMENT AND PROCEDURAL PLANNING

Anatomical variations of origin make understanding of stumpless aorto-ostial RCA CTO more complex and mandate computed tomography (CT) coronary angiogram for interventional planning [Figure 2a and b]. Antegrade options are not available in this scenario. In retrograde, after placement of the microcatheter at the distal cap, the RCA origin and course of the proximal segment should guide the wire of choice for escalation. In the regular origin with perpendicular

course from sinus, the wire can be escalated to intermediate penetration force wires like Gaia 2, 3 [Figure 2c and d] or high penetration force Conquest (Asahi Intecc, Japan) or Hornet (Boston Scientific, USA) wires if required. However, in other origins with vessels coursing along the aortic wall either upward or downward, the possibility of intermediate or high penetration force wires entering the aorta through the subintima or extra-arterial course is high. Hence, escalation to low or medium penetration force polymer jacket wires (Pilot series [Abbott Vascular, USA]) is the preferred option when channel tracking wires do not make any progress. Entry into the aorta through subintima can pose the risk of aortic dissection or aortic intramural hematoma.^[6,7] In addition to these, externalization in this scenario needs snaring [Figure 3i] of retrograde wire, preferably in the brachiocephalic artery or descending thoracic aorta if feasible.

RIGHT CORONARY ARTERY ORIGIN ANOMALIES AND ITS IMPACT ON NONOSTIAL RIGHT CORONARY ARTERY CHRONIC TOTAL OCCLUSION INTERVENTION PLANNING

Guide support is crucial for crossing the CTO segment with wire escalation that depends on the type of guide and its coaxial alignment with ostio-proximal RCA. The type of guide and guide coaxiality is determined by the origin of RCA and its subsequent course after its origin.^[8] The aforementioned RCA origin variations do not allow deep seating of guide catheter, leading to noncoaxiality and poor support for antegrade wire escalation and gear advancement. Anchor balloon [Figures 1b and 4a-c] or preemptive usage of guide extension catheter, preferably TrapLiner (Teleflex, USA) [Figure 4c], enhances guide support facilitating wire escalation and also assists in reverse CART and externalization. Antegrade dissection with knuckle wire in this scenario can only be done by balloon anchoring of microcatheter [Figure 4d and e] or by guide-extension balloon anchoring using a ping-pong guide if adequate vessel size is available proximal to CTO [Figure 4b].

MID-RIGHT CORONARY ARTERY COURSE VARIATIONS

Mid-RCA course in left anterior oblique (LAO) projection is generally perceived as “C” shape and that guides the operator in wiring CTOs in this location. This general assumption does not work every time as variations in the course of RCA as “Z” or “S” bends are common in this segment [Figures 3a, b and 5a-c]. If there is a long CTO encompassing the entire mid-RCA, a complete understanding of the course of RCA is important for wiring either antegrade or retrograde. Certain anatomical clues like the origin of acute marginal arteries [Figure 6a and b] help in ascertaining the course of the vessel in angiography.

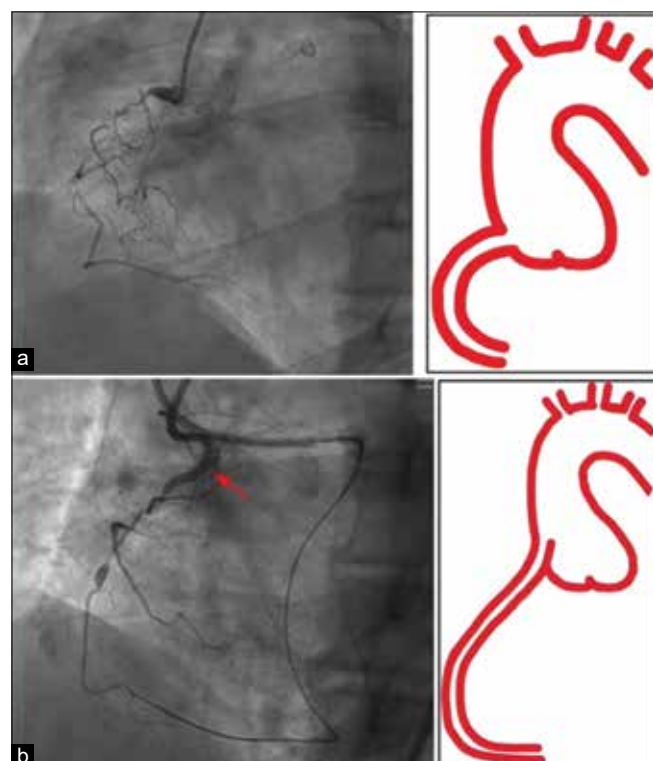


Figure 1: (a) RCA originating from anterior part of right sinus and traversing horizontally. (b) RCA originating from anterior and cranial part of right sinus and traversing downwards

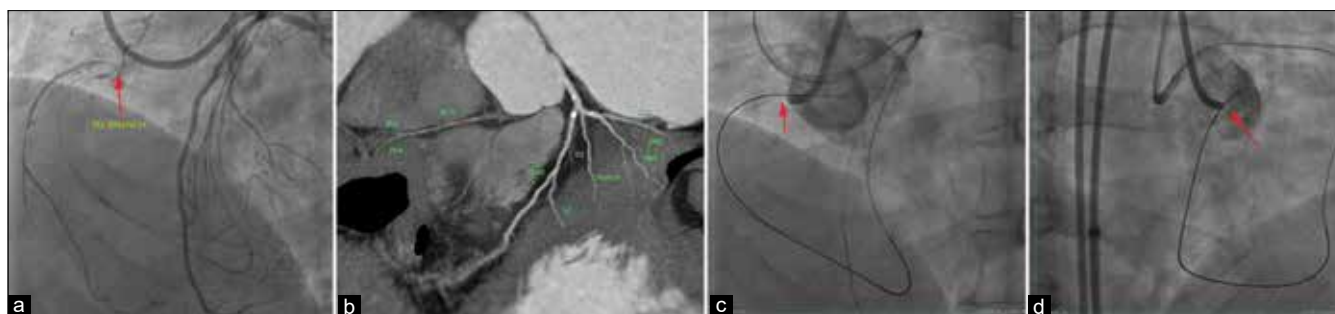


Figure 2: Stumpless ostial RCA CTO. (a and b) Angio and CT image showing short segment ostial RCA CTO and normal origin with perpendicular course of proximal RCA. (c) LAO View: Retrograde Gaia 2 Coursing horizontally towards aorta. (d) RAO view: Retrograde Gaia 2 entering aorta at mid right coronary sinus. RCA: Right coronary artery, CTO: Chronic total occlusion

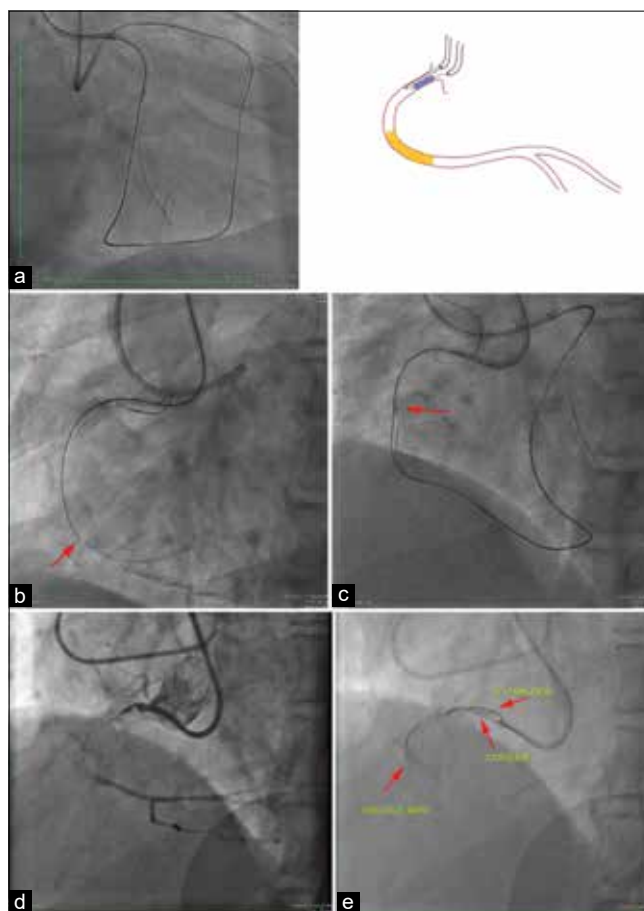


Figure 3: (a) Proximal RCA loop. (b) 1.5 mm anchor balloon in SA node branch to enhance guide support for AWE. (c) Antegrade wiring supported by guide extension and anchor balloon support. (d) Proximal to mid RCA instent CTO. (e) Knuckled wire through Corsair entrapped in proximal RCA with 3 mm balloon

However, when the course is unclear in angiography, CT coronary angiography is needed for better understanding to prepare an appropriate wiring strategy.

IMPACT OF THE BENDS ON PROCEDURAL PLANNING FOR MID-RIGHT CORONARY ARTERY CHRONIC TOTAL OCCLUSION

“Z” or “S” bends in mid-RCA result in difficulty in navigating medium-to-high penetration force wires due to unclear paths.

These bends increase the possibility of antegrade wire going subintimal or even out of vessel architecture if high HPF wires are used (Hornet 10, 14/Conquest 12,20). CT fusion into a fluoroscopy screen would guide the operator to navigate wire across the CTO body, but it is not unremarkably accurate. When the course is unclear, medium penetration force polymer-jacketed wire is a better choice for wire escalation, and parallel wire or antegrade dissection and reentry (ADR) would help in bailing out when the first wire goes subintimal. However, the threshold to go retrograde is much less in

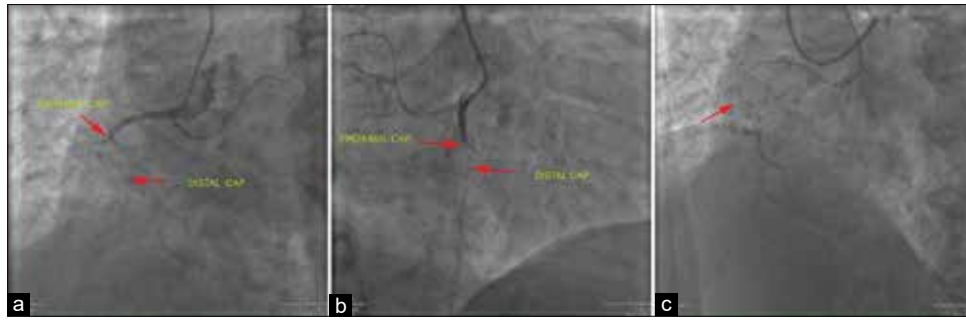


Figure 4: (a and b) Mid RCA CTO - CTO segment appeared straight in RAO view but non-linear location of caps of CTO in LAO view. (c) Fielder XTR (Asahi Intecc, Japan) wire forming a loop in the CTO segment in LAO view

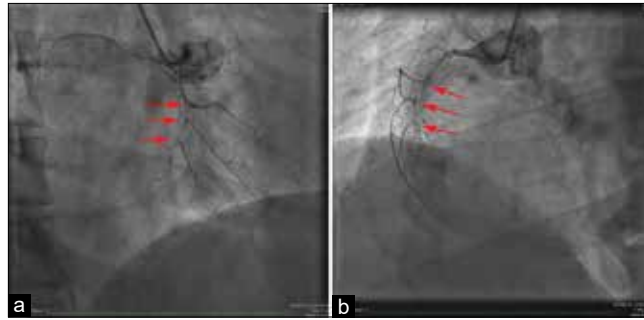


Figure 5: (a and b) Mid RCA CTO acute marginals origin delineating the course of the vessel

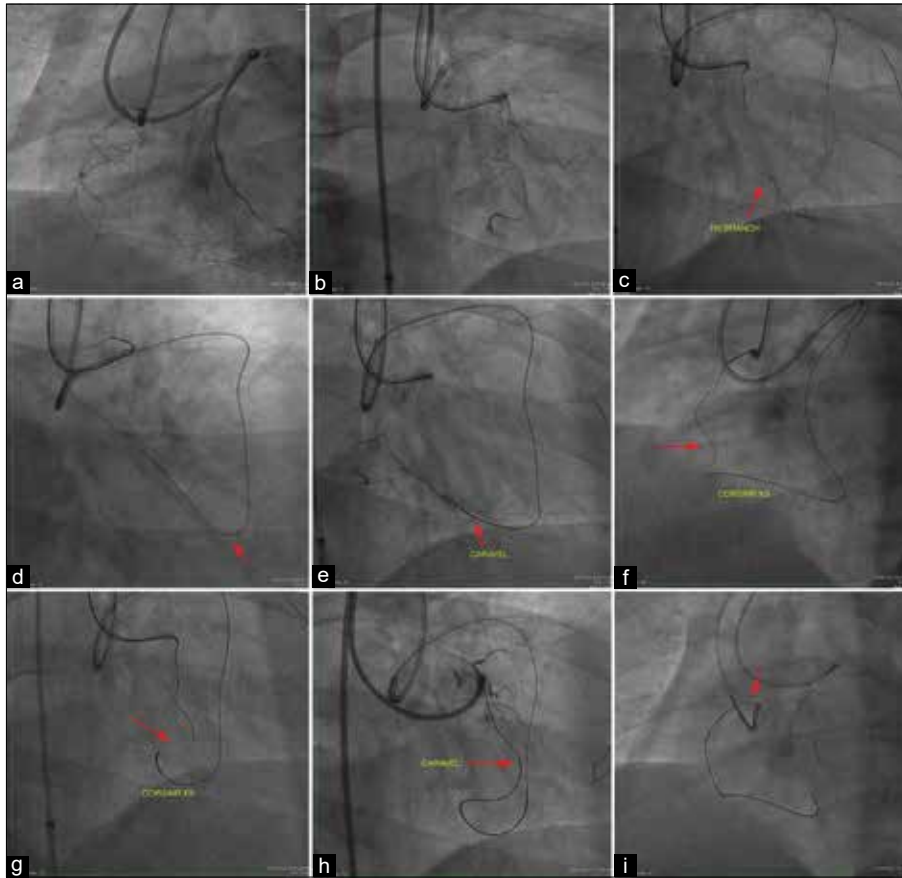


Figure 6: (a and b) S or Z bend in mid RCA with a short CTO. (c and d) Septal collateral connecting to RV branch with an acute bend at transition delineated by Caravel microcatheter (Asahi Intecc, Japan). (e) Caravel through septal into RV branch - angiogram showing short collateral entry to distal cap distance. (f and g) Loop in mid RCA transition to distal RCA in LAO and RAO view. Retrograde Corsair stuck at the loop. (h) Caravel traversed the loop. (i) Retrograde wires snaring with goose neck snare through the antegrade guide

such tortuous anatomies as two wires on either side of CTO would help in the advancement of either wire using the other as a marker. In retrograde, while choosing collateral, if the septal collateral is connected to the right ventricular (RV) branch [Figure 3c], the site of RV branch origin in relation to the distal cap [Figure 3d and e] is important as short RV branch entry to distal cap distance coupled with its increased mobility in fluoroscopy reduces maneuverability and steerability of retrograde wire. For retrograde wiring in mid-RCA bends, the microcatheter should be advanced close to the distal cap for better wire control and escalation to medium penetration force wires. If Corsair does not advance [Figure 3f and g], switch to a more flexible microcatheter like Caravel or Fine Cross (Terumo, Japan) [Figure 3h] to traverse the loops to reach the distal cap.

Furthermore, tortuosity would result in divergence of antegrade and retrograde wires, resulting in difficulty in connecting spaces [Figure 7a and b]. In case of persistent

difficulty in approximating antegrade and retrograde wires, knuckle wire can be used, preferably, retrograde knuckling to overcome the course ambiguity. Conventional reverse CART with 1:1 balloon and high tip load retrograde wire (Hornet or Conquest series) with long curve or IVUS-guided reverse CART in feasible cases would increase the success of bringing retrograde wire into antegrade space. Operators need to be mindful of all the branches of mid-RCA when ADR is considered to prevent CrossBoss (Boston Scientific, USA) or knuckle wire entry into these branches and consequent perforations. A larger knuckle can be used to cross past the side branches if CrossBoss is entering side branches. In Z or S bends, knuckle wire is the safer strategy for dissection than CrossBoss. Mid-RCA is not a good zone for reentry due to poor visibility and hypermobility.

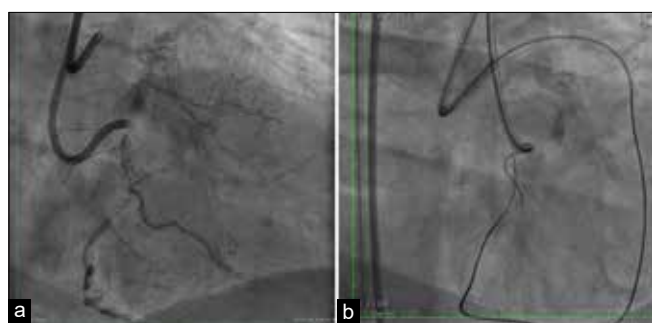


Figure 7: (a) Tortuous CTO segment in mid RCA. (b) Antegrade retrograde wires in different planes due to tortuosity

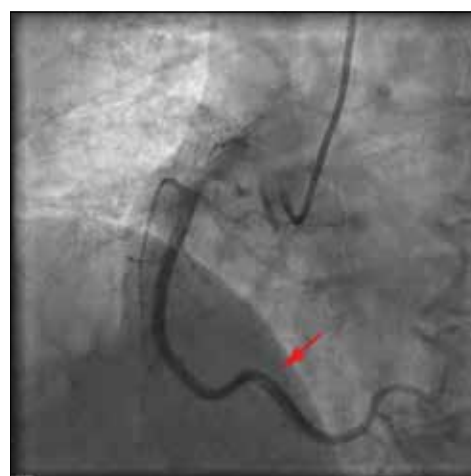


Figure 8: Sinusoidal bend in normal distal RCA in LAO projection

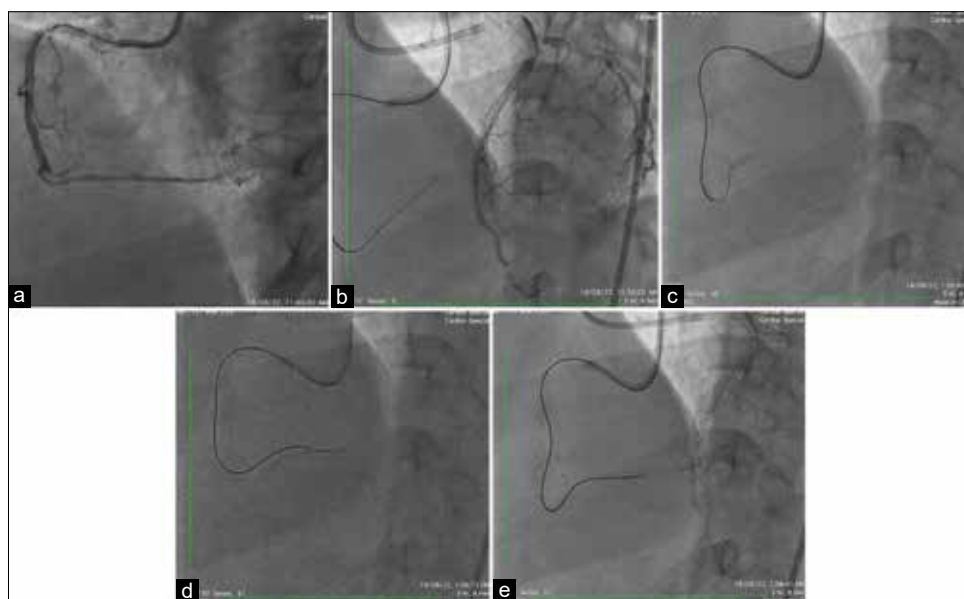


Figure 9: (a) Dual injections showing CTO of distal RCA with early origin of PDA. (b) Gaia 2 exited vessel architecture due to bend. (c) Knuckled wire with Fielder XTR beyond the proximal cap. (d) Knuckled wire across the bend till the segment of RCA which is in line with distal vessel. (e) Switch to directable wire (Gaia 2) after crossing loop with a knuckle and advancement of microcatheter

IMPACT OF THE BENDS ON PROCEDURAL PLANNING FOR DISTAL RIGHT CORONARY ARTERY CHRONIC TOTAL OCCLUSION

In this scenario, antegrade wire maneuverability is reduced, so preemptive guide extension catheter (preferably TrapLiner) placement across the loops of RCA would facilitate antegrade wire escalation (AWE). Furthermore, guide extension would simplify externalization when moved to retrograde as maneuvering high penetration force wires across these bends till the antegrade guide catheter is time-consuming and, at times, the wire may go subintimal before reaching the antegrade guide catheter. Guide extension also facilitates seamless subsequent antegrade device movement across the loops.

DISTAL RIGHT CORONARY ARTERY VARIATIONS

Distal RCA course can show similar loops [Figure 8] as mid-RCA but less frequently. Nonetheless, the site of PDA origin and its alignment with distal RCA plays a significant role in planning CTO intervention.

IMPACT OF THE BENDS ON PROCEDURAL PLANNING FOR DISTAL RIGHT CORONARY ARTERY CHRONIC TOTAL OCCLUSION

Figure 9a-c shows distal RCA CTO with the early origin of PDA. AWE to intermediate or high penetration force wires can lead to wire exiting out of vessel architecture [Figure 9b]. Even retrograde wire can exit in a similar way. Hence, the knuckle wire [Figure 9d and e] in this situation helps in clearing the path but necessitates having a reentry strategy if the knuckle goes subintimal.

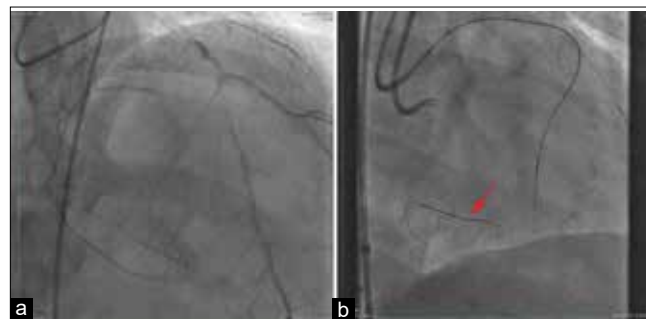


Figure 10: PDA recanalization in ADR with re-entry in PLVB

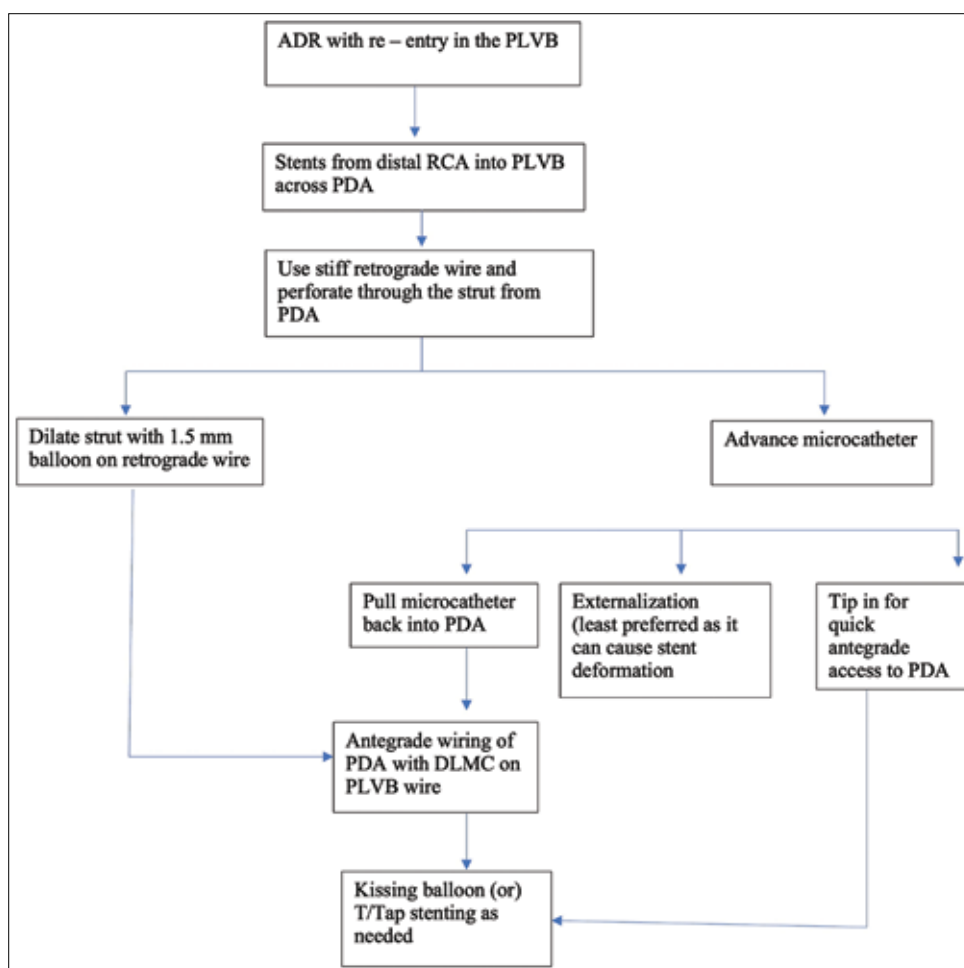


Figure 11: (a and b) Distal RCA to PDA angulation unfavourable for retrograde wire entry to distal RCA

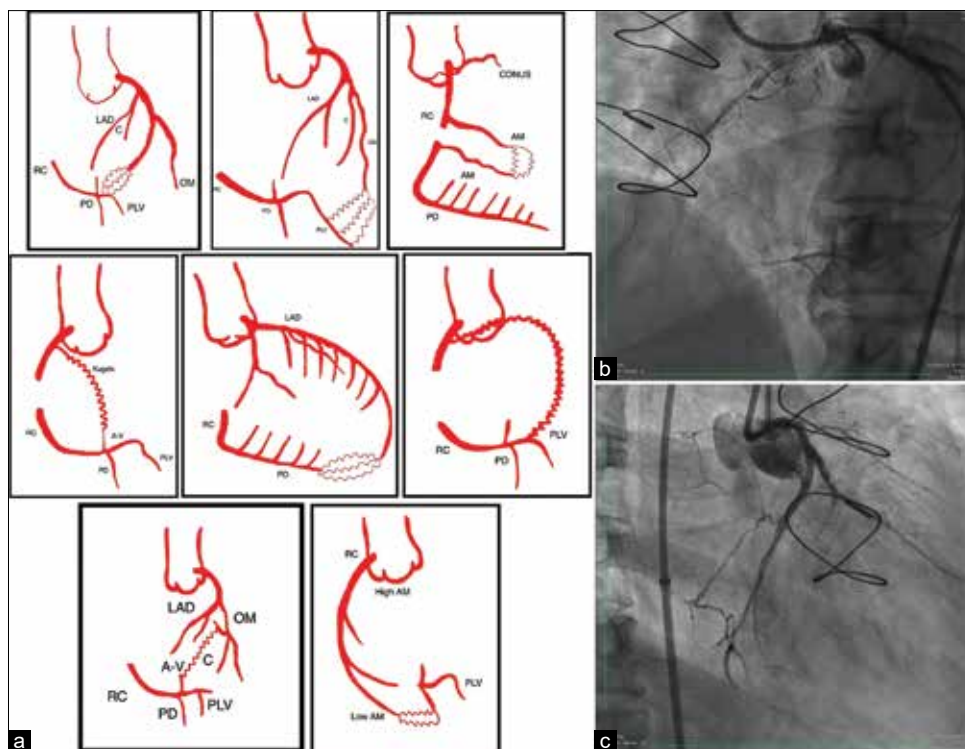


Figure 12: (a-c) Posterior AV groove epicardial collateral from LCX to PLVB

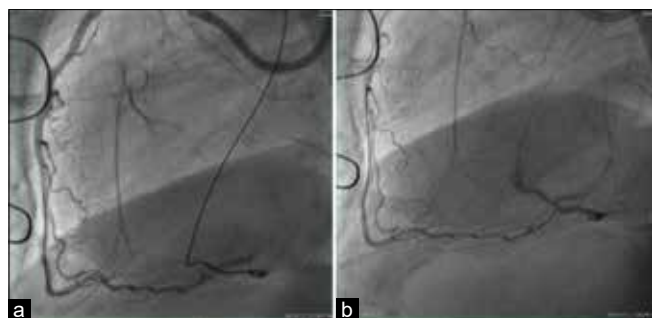


Figure 13: (a and b) SVG to distal RCA anastomose before crux. SVG is coaxially aligned to distal RCA and wire went into distal RCA

IMPACT OF THE BENDS ON PROCEDURAL PLANNING FOR PROXIMAL TO MID-RIGHT CORONARY ARTERY CHRONIC TOTAL OCCLUSION

After crossing CTO, the antegrade wire must be navigated carefully under visualization to prevent entry to subintima. However, advancing the microcatheter beyond CTO, if possible, and swapping it to workhorse wire shall simplify crossing distal tortuous RCA. Similarly, when retrograde wiring is used, the microcatheter should be placed close to the distal cap traversing the loop before escalating to intermediate or high penetration force wires [Figure 3f-h].

SEPTAL COLLATERALS AND THEIR VARIABLE COURSE AND DRAINAGE

Septal collaterals are generally safe retrograde channels but are next only to venous graft conduits.^[9,10] Crossing of septal collaterals from the left anterior descending artery (LAD) to RCA is easier than vice versa due to the favorable take-off angle. Nevertheless, septal collaterals for retrograde RCA percutaneous coronary intervention (PCI) can pose many challenges due to its variations of entry into RCA, coaxiality of the recipient branch with the distal RCA, and collateral entry to distal cap distance. In general, septal collaterals enter PDA, but infrequently, entry into RV branches is shown in Figure 3c. Unlike septals entering the PDA, those entering the RV branch would pose challenges to advance retrograde microcatheter due to the acute angle of entry and reduce wire maneuverability due to hypermobility [Figure 3d and e]. Sufficient collateral entry to distal cap distance is crucial to maneuver retrograde gear^[11] into the distal RCA. In cases of distal cap at the crux, steering retrograde gear into distal RCA becomes difficult. Further, steering wire into distal RCA is difficult if proximal PDA is not coaxial with distal RCA but aligned to posterior left ventricular branches (PLVB), as shown in Figure 10a and b. In such situations, retrograde double-lumen catheter (Sasuke, Asahi Intecc) would offer some support for wire navigation; However, ADR or marker wire technique can be used to navigate antegrade wire

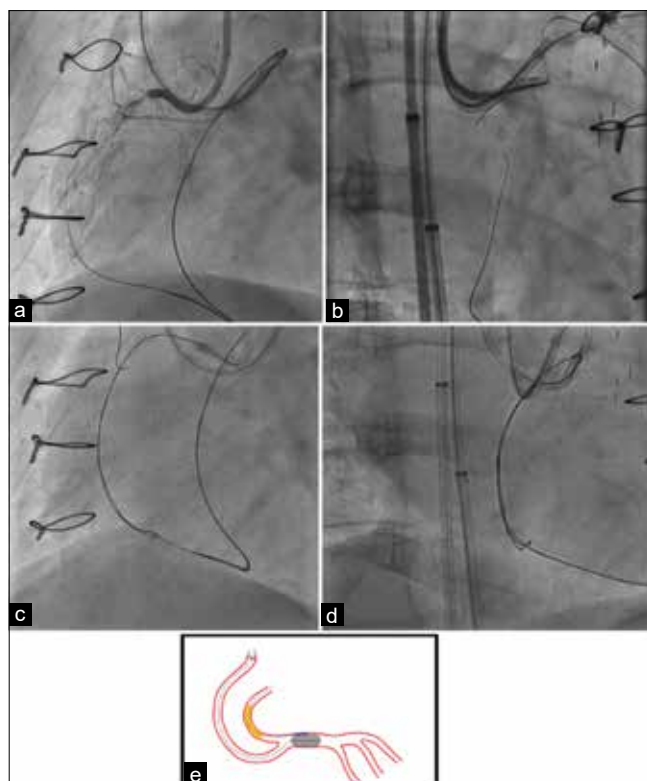


Figure 14: (a and b) Retrograde wire appearing as if in RCA in LAO view but in RAO view wire positioned was anterior to RCA suggestive of SVG. (c and d) Retrograde wire in RCA in LAO and RAO views. (e) Facilitated ADR

into PLVB. If reentry is in PLVB, PDA can be rescued using techniques described in Figure 11.

EPICARDIAL COLLATERALS OF RIGHT CORONARY ARTERY

RCA is supplied with a variety of epicardial collaterals, both ipsilateral and contralateral, based on the location of CTO, as depicted in Figure 12a-c. Among them, posterior AV groove and distal LAD to PDA collaterals are often used for retrograde interventions as the size is conducive. Determine the better view for visualization of the channel before embarking on wiring it. Certain nuances must be kept in mind when distal LAD to PDA epicardial collateral is chosen, use short guides to get the more usable length of microcatheter and use antegrade guide extension catheter for externalization. AV groove collaterals are preferred over septal when angulation of PDA at the crux is noncoaxial with distal RCA and distal cap to PDA origin distance is too short for wire maneuvering. When AV groove collaterals are used in postcoronary artery bypass graft patients, the threshold for embolization is much lower if perforated, as it might lead to a loculated tamponade of LA.^[10,11]

RIGHT CORONARY ARTERY GRAFTS AS CONDUITS

RCA is grafted with either venous or arterial grafts based on the availability of conduit, age of patient, and choice of

surgeon. In general, venous grafts are the safest retrograde conduits.^[12] Crossing occluded venous grafts becomes difficult with a longer duration of occlusion. Graft characteristics that affect technical decisions while using it as retrograde conduit are aortic anastomosis site, lie of the graft, distal anastomosis site, and angulation of the distal part of saphenous vein graft (SVG) with the recipient vessel proximal to anastomosis.

Proximal anastomosis of SVG is generally done on the right anterior aspect of the aorta. Guide selection is the key, as retrograde catheter advancement needs good support. Judkins right, multipurpose, Amplatzer left, or right venous bypass cannulates SVG based on the site of anastomosis on the aorta and the angulation of proximal graft with the aortic wall. The course of the venous graft depends on the site of distal anastomosis and the length of the graft. Distal anastomosis is generally done in distal RCA territory to [Figure 13a and b] proximal PDA, proximal PLVB or rarely on to RV branches of good size. Usually, surgeons prefer the graft to be coaxial with the distal recipient for favorable flow dynamics, which makes graft angulation with the proximal vessel more acute. This kind of angulation would make retrograde wire navigation into proximal RCA a bit challenging, especially when graft length is short, as it makes the angle more acute.^[13-15]

In retrograde RCA PCI through septal collateral with occluded venous graft anastomosed to distal RCA, the operator should navigate through pre-crux RCA in both LAO and right anterior oblique (RAO) views as plain LAO does not differentiate wire course in RCA from that in SVG [Figure 14a-d].^[16]

The availability of SVG conduit in native RCA CTO PCI increases the success of reentry by facilitated ADR^[17] [Figure 14e]. In this, a balloon of 1:1 size is inflated at the reentry site, followed by reentry through Stingray (Boston Scientific, USA) using stick and drive technique with Gaia 2/3, Conquest, or Hornet wires.

CONCLUSION

RCA is the common host for CTO and also for anatomical variations, which complicates CTO interventional planning. The anatomy of the CTO segment plays a major role in preparing the wiring strategy, but the vessel proximal and distal to the CTO also determines the success by influencing the navigability of antegrade or retrograde gear. Hence, a comprehensive idea of the anatomy of the entire RCA from its origin to bifurcation at the crux would help in suitable collateral selection and preparing an appropriate bailout strategy for anticipated problems. Understanding RCA tortuosity in CTO or non-CTO segments and the site of origin of branches within respective segments helps in tailoring ADR and choosing the site and the type of reverse CART.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

Efficacy and safety of tenecteplase as bridging therapy in large vessel occlusions: A retrospective observational study

ABSTRACT

Background and Objectives: Clinical trials showed a higher recanalization rate of tenecteplase (TNK) over alteplase in large vessel occlusion (LVO) and better functional independence at the end of 3 months without increasing the risk of systematic intracranial haemorrhage (SICH). Indian data on the efficacy of tenecteplase as bridging therapy in LVOs are scarce. We aimed to review the outcomes and safety of tenecteplase up to 4.5 h in LVO patients who were taken for mechanical thrombectomy (MT).

Methods: This is a single-center retrospective study. Patients with acute ischemic stroke who had LVO and were taken to an angiographic suit for MT were included in the study. Other inclusion criteria were an age of more than 18 years, National Institute of Health Stroke Scale >4, modified Rankin score (mRS) of 2 or less before stroke, and no evidence of hemorrhage on noncontrast computed tomography of brain. The primary efficacy outcome was mRS score of 0–2 at the end of 3 months. Development of symptomatic intracerebral hemorrhage was considered the primary safety outcome.

Results: A total of 27 patients were included in this study. The mean age of presentation was 61 years. Most of the study subjects were males 59.25%. Hypertension was the most common risk factor seen in 19% (70.37%) of subjects. About 11 patients (40.74%) had M1 occlusion, 6 (22.22%) subjects had M2 occlusion, 8 (29.62%) patients had internal carotid artery occlusion, and 2 (7.4%) subjects had basilar occlusion. Early recanalization with IV thrombolysis (IVT) was noted in 5 (18.51%) of patients after IVT with tenecteplase. Functional independence (mRS: 0–2) was achieved in 15% (55.55%) of patients. Symptomatic intracranial hemorrhage was seen in 1 (3.7%) subjects and death within 90 days is noted in 3/27 (11.11%) subjects.

Conclusion: Tenecteplase is appearing to be an effective bridging agent before MT in LVOs considering its ease of administration, low cost, effective recanalization rates, and good functional recovery.

Keywords: Alteplase, mechanical thrombectomy, tenecteplase

INTRODUCTION

Worldwide, stroke ranks as the second leading cause of death and the third leading cause of composite death and disability.^[1] Acute ischemic stroke (AIS) constitutes 85% of stroke cases. Novel treatments such as IV thrombolysis (IVT), and more recently, mechanical thrombectomy (MT) for large vessel occlusion (LVO) have reduced mortality by 10% compared with the older treatments and improved long-term disability prevention rates after AIS.^[2,3] AIS management guidelines recommend intravenous thrombolysis with the tissue plasminogen activator alteplase within 4.5 h after the onset of stroke and MT within 24 h after onset.^[4,5] Accumulating evidence from clinical trials suggests that

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tenecteplase may represent an effective treatment agent compared with alteplase for AIS.^[6,7] In a recently published Randomized controlled trial (RCT), tenecteplase administration was associated with a 2-fold increase in the odds of successful recanalization of AIS patients with LVO before the initiation of endovascular treatment compared with patients receiving pretreatment with intravenous alteplase. Patients randomized to intravenous tenecteplase before endovascular treatment also had better functional outcomes at 3 months compared with patients receiving intravenous alteplase.^[8] TNK has several advantages that make it an appealing and effective agent, it is generally cost-effective, has a high fibrin specificity and longer plasma half-life, enhanced plasminogen activator inhibitor-1 resistance, and can be dispensed as a single bolus, making it applicable in the prehospital settings.^[9] Indian data on the usage of tenecteplase in LVOs before MT are sparse. In this study, we aimed to review the efficacy and safety of tenecteplase in LVOs as bridging therapy before MT in our center.

METHODS

This was a single-center, retrospective, observational study. We have studied a cohort of patients who received tenecteplase as a bolus dose for AIS secondary to LVO before taking to angiographic suit for MT. Patients were enrolled between April 1, 2021, and March 30, 2023.

Inclusion and exclusion criteria

All the patients of AIS who presented within 4.5 h of onset of symptoms, had LVO (defined as middle cerebral artery [M1, M2], internal carotid artery [ICA], CCA, and basilar occlusions), underwent thrombolysis with tenecteplase, and taken to angiographic suit for MT. Other inclusion criteria were an age of more than 18 years, a deficit with National Institute of Health Stroke Scale (NIHSS) score >4, a modified Rankin score (mRS) of 2 or less before the stroke onset, and no evidence of hemorrhage on noncontrast computed tomography (CT) imaging of brain. Patients with contraindications for thrombolysis were excluded from the study. A written informed consent for thrombolysis and thrombectomy was obtained from the patient wherever feasible or else by the close relative. The consent included a detailed explanation of the benefits and risks associated with stroke thrombolysis and MT are obtained.

Data entry and retrieval

The demographic, clinical, and imaging details of all the patients for whom the emergency stroke code is activated are prospectively entered into our hospital-based central

stroke data register. The stroke timeframes including onset to door, door to CT and door to needle times, and door to groin puncture were entered by the attending ER physician and neuro interventionist. We performed a retrospective data sorting and retrieval of the stroke patients who underwent recanalization therapies according to the defined inclusion and exclusion criteria.

Drug administration

Patients were administered 0.25 mg/kg of tenecteplase as single bolus intravenously over 5 s.

Angiographic evaluation and mechanical thrombectomy protocol

All the ischemic stroke patients in our study underwent an urgent baseline magnetic resonance imaging (MRI) brain and TOF MR angiography of intracranial vessels. Patients in whom MRI could not be done, CT brain and CT angiogram of intracranial and extracranial vessels were done. The patients who had intracranial LVOs were immediately shifted to the catheter laboratory for digital subtraction angiography (DSA). The patients receiving tenecteplase were shifted after getting the bolus dose according to the aforementioned protocol. MT was performed in patients confirmed to have an LVO on DSA. Informed consents were obtained before performing DSA and MT.

Outcome measures

Early recanalization noted in the angiography suit and good functional recovery (mRS score of 0–2) at the end of 3 months was defined as the primary efficacy outcome. The functional recovery in follow-up visits including the one at 3 months was assessed by the neurologist. The primary safety outcome was assessed by analyzing patients with symptomatic intracerebral hemorrhage (defined as any fresh intracranial bleeding resulting in a decline of NIHSS >4 points or death) within the first 24 h after administration of thrombolytic agent. All patients underwent a follow-up brain imaging after 24 h of receiving thrombolytic therapy. Further, the patients with a neurological deterioration causing any measurable worsening on NIHSS score underwent an immediate CT brain imaging to rule out hemorrhage.

Statistical analysis

Statistical analysis was conducted using IBM. SPSS version 23.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were computed as percentages, while continuous variables as mean \pm standard deviation mRS being an ordinal scale variable, its values were analyzed as median. One-way ANOVA test was used for comparing categorical variables. All $P < 0.01$ were considered significant.

RESULTS

A total of 27 patients underwent intravenous thrombolysis with tenecteplase and were taken to angiographic suit for DSA, followed by MT during the study period. The baseline characteristics of the patients are shown in Table 1.

Efficacy and safety outcome parameters

The recanalization after IVT with good distal flow (TICI2B/3) was seen in 5 (18.51%) patients. Median mRS score at 3 months of follow-up was 2. The good functional recovery at 3 months with mRS 0–2 was observed in 55.5% of patients. The total number of patients who had symptomatic intracranial hemorrhage was 1 (3.7%) [Figure 1]. Total number of deaths related to stroke in 3 months was 3 (11.11%). Total of 3 (11.11%) patients underwent decompressive hemicraniectomy. None of the patients had access site complications [Table 2].

Characteristics of patients who had recanalization with IV thrombolysis

A total of five patients with LVO had recanalization after IVT, out of which two patients had M2 occlusion, two patients had M1 occlusion, and one patient had ICA occlusion. Three of these five patients underwent thrombolysis within 3 h of onset of symptoms [Table 3].

DISCUSSION

In this single-center retrospective study of patients with AIS with LVO, intravenous thrombolysis with tenecteplase before endovascular thrombectomy is observed to be effective and safe. The recanalization rates in the present study are 18.51% when compared to recanalization rates with alteplase in LVO in other studies such as ESCAPE trial 5.1% (7/118) and^[10] MR CLEAN-NO IV 3.7% (9/245).^[11] Symptomatic intracranial hemorrhage in the ESCAPE trial was 6/165 (3.6%), in MR CLEAN-NO IV 14/266 (5.3%), in alteplase, followed by EVT group, in the present study, SICH is 1/27 (3.7%) which is comparable with above two RCTS. In the MR CLEAN-NO IV trial, death within 90 days in 42/266 (15.8%, in alteplase, followed by EVT group), in the ESCAPE trial, death within 30 days 44/233 (18.9%) in the intervention group, in the present study, death within 90 days is 3/27 (11.11%) which is comparable with the above two RCT. The higher recanalization rates of patients in the present study could be attributed to the higher fibrin specificity and more potent clot dissolution with tenecteplase^[12] leading to faster vessel recanalization. The tenecteplase can be administered as a single bolus injection compared with alteplase which requires 1 h infusion after initial bolus.^[12,13] The ease of tenecteplase administration

constitutes an indisputable advantage in the acute stroke setting, enabling prompt AIS treatment in the emergency department or even in an ambulance. The clinical benefit of tenecteplase compared with alteplase has been reported

Table 1: Baseline characteristics of patients

Characteristics of the patient	n=27, n (%)
Age (years), mean ±SD	61 ± 15.04
Gender (male)	16 (59.25)
Risk factors	
Type 2 DM	14 (51.85)
HTN	19 (70.37)
CAD	7 (25.29)
Dyslipidemia	12 (44.44)
CKD	4 (14.81)
Rheumatic heart disease	3 (11.11)
NIHSS score on arrival	
<5	0
5–10	2 (7.4)
11–20	19 (70.37)
>20	6 (20.68)
Onset to IVT time	
IVT in 0–3 h	11 (37.93)
IVT in 3–4.5 h	14 (51.85)
Unknown time of onset	2 (7.4)
Drip and ship (received IVT outside our hospital)	4 (14.81)
Onset to groin puncture time	
Onset to groin time up to 6 h	16 (59.25)
Onset to groin time beyond 6 h	9 (33.33)
Diffusion/CT aspect	
<6	3
6–8	22
>8	0
LVO	
M1	11 (40.74)
M2	6 (22.22)
ICA	8 (29.62)
Basilar artery	2 (7.4)

SD: Standard deviation, NIHSS: National Institute of Health Stroke Scale, DM: Diabetes mellitus, HTN: Hypertension, CAD: Coronary artery disease, AF: Atrial fibrillation, CKD: Chronic kidney disease, DLP: Dyslipidaemia, LVO: Large vessel occlusion, MCA: Middle cerebral artery, ICA: Internal carotid artery, CT: Computed tomography, IVT: Intravenous thrombolysis

Table 2: Efficacy and safety outcomes table

Efficacy outcomes	n=27, n (%)
Recanalization after IVT (0–4.5 h)	5 (18.51)
Received IVT in 3 h	5 (18.51)
Received IVT in 3–4.5 h	2 (7.4)
Recanalization after MT	18 (66.66)
Functional independence MRS (2 ≤) at 3 months	15 (55.55)
Any hemorrhage	4 (14.81)
Symptomatic hemorrhage	1 (3.7)
DECRA	3 (11.11)
Death	3 (11.11)
Access site complications	0

IVT: Intravenous thrombolysis, MT: Mechanical thrombectomy, MRS: Modified Rank in score

to be more pronounced for patients with viable penumbra and considerable mismatch in baseline neuroimaging,^[13] providing further support to the hypothesis that earlier and more complete tenecteplase-induced reperfusion in patients. In an Indian study, TENVALT^[14] which compared two thrombolytic agents TNK and alteplase, a total of 45 patients received TNK of which 18 patients had LVO of which 3 patients (16.6%) had early recanalization during the digital subtraction angiogram. In EXTEND 1A TNK part 2,^[15] a randomized controlled study comparing 0.25 mg versus 0.4 mg dosage of TNK in LVOs, a total of 150 patients received 0.25 mg TNK. In EXTEND 1A TNK part 2 trial, 19.3% (29/150) of subjects had early recanalization, 56% (84/150) of patients had functional independence at the end of 3 months, and 1.3% (3/150) had symptomatic hemorrhage. In the present study, we observed early

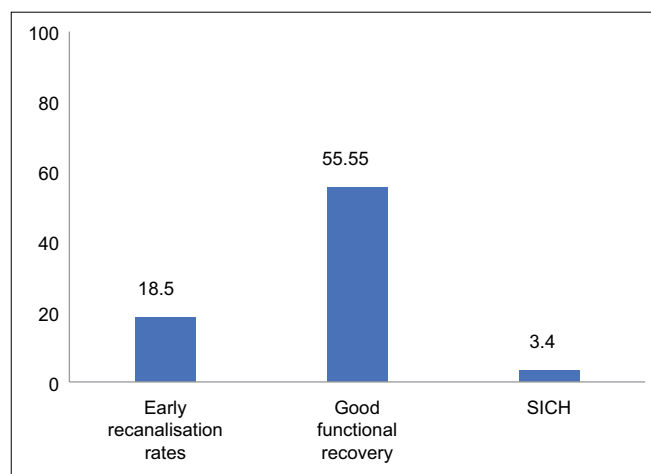


Figure 1: Chart representing primary efficacy and safety outcomes

Table 3: Characteristics of patients who had recanalization with IV thrombolysis

Age	Onset to IVT time	LVO	Onset to groin time
28	3 h 45 min	M2	5 h
40	2 h 15 min	M2	4 h
72	45 min	ICA	7 h 15 min
55	1 h 45 min	M1	2 h 30 min
55	2 h 50 min	M1	4 h 15 min

IVT: Intravenous thrombolysis, LVO: Large vessel occlusion, ICA: Internal carotid artery

Table 4: Comparison of the present study with EXTEND 1A TNK part 2 study

Study	Study design	Recanalization rates (%)	Functional independence at 3 months mRS of 0–2 (%)	Symptomatic hemorrhage (%)	Results
EXTEND 1A TNK part 2 (0.25 mg group)	RCT	29/150 (19.3)	84/150 (56)	2/150 (1.3)	0.25 mg/kg TNK is as efficacious as 0.4 mg/kg in LVO
Present study	Retrospective observational	5/25 (18.5)	15/27 (55.55)	1/27 (3.7)	Early recanalization rates of 18.5%, functional recovery of 55.55% are comparable with other TNK trials and better than alteplase, with a SICH rates of 3.4%

LVO: Large vessel occlusion, mRS: Modified Rank in score, TNK: Tenecteplase, SICH: Systematic intracranial haemorrhage

recanalization rates with IVT were 18.51% (5/27), functional independence at the end of 3 months to 55.55% (15/27) which is comparable to EXTEND 1A TNK part 2 trial. In our study, symptomatic hemorrhage rates are 3.7% (1/27) which is similar to 1.3% (2/150) SICH rates of EXTEND 1A TNK part 2. Death within 90 days in the EXTEND 1A part 2 trial is 22/150 (15%, TNK 0.25 mg group), in the present study, death within 90 days is 11.11% (3/27) which is comparable with the above RCT.

In a systemic review and meta-analysis done by Katsanos *et al.*,^[16] it was found that AIS patients with LVO receiving intravenous thrombolysis with tenecteplase have three-fold higher odds of achieving successful recanalization and two-fold higher odds of having favorable clinical outcomes at 3 months compared with patients receiving intravenous alteplase. The above meta-analysis is a review of the Australian TNK trial^[17] and EXTEND 1A TNK trial.^[8]

In the present study, four patients received TNK in the drip-and-ship model, of whom one patient had early recanalization noted in the angiographic suit. A recent French report highlights that tenecteplase and alteplase may yield similar complete recanalization rates (21% vs. 18%) in LVO patients pretreated with intravenous thrombolysis in the drip-and-ship setting.^[18] There are few limitations in our study such as small sample size, single-center retrospective study, and no comparative data with alteplase. A large-scale multi-centric prospective randomized study with tenecteplase and alteplase as bridging agents in our clinical settings would be ideal to test the hypothesis of better bridging thrombolytic agents before MT in LVOs.

CONCLUSION

In view of the lower cost and ease of administration, higher early recanalization rates, and better functional outcomes, tenecteplase may have great potential as a bridging therapy in LVOs before MT. Because of the ease of administration, it is enormously helpful in the drip-and-ship model before being shifted for MT in LVO.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Original Article

Role of food choice for breast cancer prevention in developing societies: A pilot case–control study in the women North Cyprus

ABSTRACT

Background: Breast cancer incidence is increasing in developing societies. The Mediterranean eating regimen has been suggested to play a preventive role in reducing breast cancer risk.

Objective: This study investigated the preventive role of fruits and vegetables, eggs, fish, olives and olive oil, and fresh potatoes consumption similar to western Mediterranean diets on breast cancer development in the women of North Cyprus.

Materials and Methods: This case–control study was carried out in Dr. Burhan Nalbantoglu Devlet Hastanesi, Lefkosa, North Cyprus. The study group was 305 women with confirmed cases of breast cancer and the control group was 302 women without breast cancer. Due consent to participate in the study was obtained. Information on dietary intake was collected, which included age, menopausal status, breast density, age at menarche, and dietary consumption of fresh potatoes, fruits and vegetables, olives and olive oil, fish, and eggs. Logistic regression model was used to analyze the link between the dietary intake and breast cancer risk.

Results: Consumption of fruits and vegetables, olives and olive oil 5 or more servings per day, and fish 2 servings per week showed an odd ratio (OR) = 0.09 (0.04–0.18), 0.06 (0.03–0.16), and 0.04 (0.02–0.10), respectively, with the 4–6 eggs per week and 4 or more servings of fresh potatoes per week OR = 0.10 (0.54–0.20) and 0.15 (0.08–0.28), respectively.

Conclusion: The consumption of olives and olive oil 5 or more times, and fish 2 or 1 times weekly played a more significant role in reducing the risk of breast cancer in women. Investigating at a larger scale in the study population is yet to be done.

Keywords: Breast cancer, breast cancer prevention, developing societies, Mediterranean diets

INTRODUCTION

Breast cancer is the most predominant malignancy among the women of North Cyprus^[1] as well as in similar developing societies.^[2] Yearly, worldwide deaths from breast cancer are about 327,000. It is estimated that 1.35 million new cases will be observed each year and in 2020, 1.7 million cases are going to be diagnosed with more than 50% of the cases in developing regions.^[3]

The increase in breast cancer risk is suggested to be due to changes in lifestyle, reproductive factors, increased life expectancy,^[4,5] genetic factors, race, environmental conditions, physical activity, socioeconomic status, body mass index, and nutrition.^[6]

Among all primary preventions for breast cancer in developing societies, the consumption of the

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right foods is the most cost-effective cancer preventive intervention.^[7]

Inter-societal differences in response to dietary consumption and breast cancer risk maybe linked to genetics.^[8] There are polymorphisms in the interactions of diets intake and gene, that may influence epigenetics and further modify the expression of genes that influence the risk of breast cancer.^[9]

A French cohort study reported, that there was an inverse relationship with breast cancer risk following the intake of “healthy/Mediterranean diet” consisting of fruits, raw or cooked vegetables, fish and crustaceans, olive oil, and sunflower oil in postmenopausal women especially those with estrogen receptors positive/progesterone receptors negative tumors^[10] and breast cancer was also observed to decrease in Latino and non-Latino Caucasian women in a study carried out in the United States to investigate the function of Mediterranean diets such as alcoholic beverages, chicken, seafood, vegetables, green salads, olive oil, and salad oil among this group.^[11] Although the study by Bessaoud et al. reported no association between breast cancer risk and the intake of fruits, raw and cooked vegetables, fish, and olive oil in France,^[12] Demetriou *et al.* in another study observed a positive relationship between the consumption of the Mediterranean diet and breast cancer risk in women.^[13] Further investigation on the Mediterranean dietary intake and breast cancer risk carried out among Greek-Cypriot women, reported that the adherence to a dietary pattern rich in vegetables, fish, legumes, and olive oil may favorably influence the risk of breast cancer.^[14] The foods consumed in the Mediterranean reduce breast cancer risk^[15] and diets of a sort conventional in Mediterranean societies are portrayed by a high intake of vegetables, fruits, fish, olive oil, and moderate consumption of protein, which are thought to present health advantages.^[15]

The defensive role of Mediterranean foods on breast cancer is biologically plausible with the Mediterranean diet rich in fiber, antioxidants such as flavonoids, vitamins, carotenoids, and squalene, and the diets might modulate breast cancer risk by diminishing endogenous estrogens,^[16] increasing sex-hormone binding globulin levels,^[17] neutralizing free radicals and preventing deoxyribonucleic acid damage,^[18,19] lessening oxidative stress,^[20,21] and genetic modification.^[22]

Previous studies on Mediterranean foods and breast cancer have provided mixed results. North Cyprus has a typical western Mediterranean way of life with living conditions and diets that ought to be ideal for healthy wellbeing.^[23,24] Culture may drive the consumption of certain types of foods in high amounts based on local availability.^[25] Limited evidence exists that supports the probable causal role of Western

Mediterranean diets. Finding the specific foods that have a significant impact on breast cancer risk will allow for a targeted consumption to achieve maximum benefits.

Furthermore, an awareness on the pivotal role of Mediterranean foods should be encouraged, most especially in the population vulnerable to micronutrients deficiencies^[26,27] such as in developing societies.

The purpose of our study was to investigate the potential positive impact of the Western Mediterranean dietary lifestyle through investigating the significance of the varying amount of intake of fruits and vegetables, fish, olives and olive oil, fresh potatoes (cooked), and eggs on breast cancer risk among the women of North Cyprus.

MATERIALS AND METHODS

General study details

This was a hospital-based case–control study. The study was carried out in Dr. Burhan Nalbantoglu Devlet Hastanesi, Lefkosa, North Cyprus, between January 2018 and November 2018. Ethical approvals were obtained from Near East University, North Cyprus ethical community with approval number YDU/2018/55-523 and the ethical community of Dr. Burhan Nalbantoglu Devlet Hastanesi, Lefkosa, North Cyprus with approval number YTK.1.01.

Informed consent was obtained from participants before the study was carried out.

There was no form of funding received for this study.

The study was conducted according to ethical guidelines established by the Declaration of Helsinki and other guidelines such as Good Clinical Practice Guidelines and those established by the ICMR.

Participants

From sampling the women enrolled were as follows:

Case group = 305 women with confirmed cases of breast cancer.

Hospital-based control groups = 302 women without breast cancer attending the cancer hospital for other reasons. Women between the ages of 18–69 years were included in the whole study group. Women with confirmed cases of breast cancer were included in the case group, while women with a history of lobular and ductal carcinoma *in situ* were excluded from the control group. Hospital-based controls were used to obtain a more reliable data.

The sampling size was based on the following calculations:

$$n = \frac{N \times t^2 \times p \times q}{(N - 1) d^2 + t^2 \times p \times q}$$

Equation 1: Equation 1 was used to determine how many women are needed to get results that reflect the target population as precisely as possible. $N = 121,257$ women population size, $t = t$ -table value = 1.96 ($\alpha = 0.05$), $P =$ (prevalence rate) = $91/100,000 = 0.00091$ (expected frequency). This is the proportion of the population affected by BC, $q = 1 - p = 0.99909$. This is the proportion of the population not affected by BC, $d =$ (acceptable margin of error) = 0.001 . The margin of error is the amount of error that can be tolerated. A lower margin of error requires a larger sample size. Following the calculations, the required sample size was 317.8 women.

Objectives

The influence of the Mediterranean diets in the prevention of breast cancer among the women of North Cyprus was studied.

Study methodology

Breast cancer cases were approached while waiting for their oncologist appointment or while receiving chemotherapy. Patients with breast cancer were selected as diagnosed pathologically based on the international classification of diseases for oncology 3rd edition (C50.0–C50.9)^[28] and registered with the cancer center’s database.

The hospital-based controls were women attending the hospital for other reasons and had no history of breast cancer. The goals of the study were explained clearly to them and due consent to participate was verbally obtained or by filling a consent form. The controls were asked questions about their dietary intake in the past 5–10 years, while the cases were also asked the same questions about their dietary intake 5–10 years before diagnosis.

Data were collected with the use of a specially designed questionnaire through a standardized interview. The questionnaire included information on age, menopausal status, age at menarche, and breast density. In addition, a diet interview was conducted on each subject using a food frequency questionnaire designed to capture the consumption of 5 food items selected from previously validated questionnaires,^[29,30] and commonly consumed by the people of North Cyprus. The frequency of intake of the 5 food items was categorized as follows: eggs intake: 4–6/week, 1–3/week and none; fruits and vegetables intake: 5 or more servings per day, 3–4 servings per day, 2 servings per day and none; olives and olive oil intake: 5 or more servings

per day, 3–4 servings per day, 2 servings per day and none; fish intake: 2 servings per week, 1 serving per week, and never; and fresh potatoes: 4 or more servings per week, 2–3 servings per week, and 1 serving or none per week. Only the completely answered questionnaires were analyzed [Table 1].

Table 1 shows the standard used for the servings of each studied Mediterranean food.^[31–33] A serving is equal to the quantity per meal and this can be cooked, fresh, or dried.

Statistical analysis

Women’s age, menopausal status, breast density, age at menarche, and dietary intake between cases and controls were first analyzed by cross-tabulation and Chi-square test. The statistical significance was $P < 0.05$. To analyze the link between the frequency of dietary intake and breast cancer risk, a multivariable logistic regression model was used and only diet consumption frequency was analyzed. No confounding variables were used in the analysis. The fit of the model was assessed on the basis of Pearson’s Chi-square or Hosmer–Lemeshow goodness of fit. The statistical analysis was carried out using IBM SPSS (IBM, Armonk, NY, USA).

RESULTS

Study flow diagram

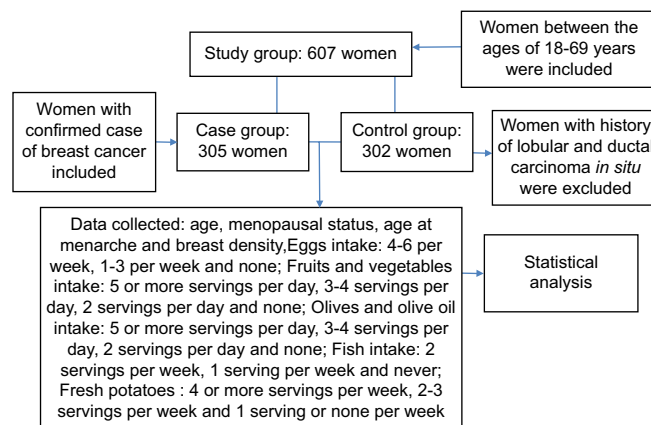


Table 1: The standard serving of the studied foods

Foods	Amounts
1 serving of vegetables	1 cup of raw leafy vegetables, 1/2 a cup of raw or cooked vegetables
1 serving of potatoes	1 cup of diced, mashed or medium-sized boiled potato
1 serving of fruits	1 cup of chopped fruits, 125 mL (1/2 cup) of fruit juice (no added sugar) and 1/2 cup dried fruits
1 serving of fish	1 can of fish, 1 cup of sliced fish, or 1 fish
1 serving of egg	1 egg
1 serving of olive oil	1 tablespoon per meal
1 serving of olives	5 olives per meal

A total of 305 breast cancer cases and 302 hospital-based controls were studied.

The age range of the participants studied was between 18 and 69 years, with a mean age of 45.60 years.

The highest number of 221 women in the menarche group were premenopausal women with 13 years of age at menarche, while the following are 163 postmenopausal women in the same category. The lowest, which is 29 premenopausal women had their menarche at age = <12 years. Fifty postmenopausal women had their menarche at age = <12 years. The women with menarche at age = >14 were 88 premenopausal women and 56 postmenopausal women.

201 women, with heterogeneously dense breast were premenopausal, followed by 155 postmenopausal women with almost entirely fatty breast and 7 postmenopausal women with extremely dense breast. Fifty-two premenopausal women had extremely dense breast [Table 2].

As shown in Table 3, more women in the hospital-based control group consumed fruits and vegetables 5 or more servings per day ($n = 161$) with less women in the breast cancer group consuming the same amount ($n = 106$).

Olives and olive oil were highly consumed in the hospital-based controls group with 49 women consuming 5 or more servings per day and 41 women in the breast cancer cases group. The number of women not consuming olives and olive oil increased in the breast cancer cases group while the reverse was the case in the hospital-based control group.

Eighty-three breast cancer cases consumed 2 or more servings per week of fish while 160 hospital-based controls consumed the same amount. One hundred and nineteen breast cancer cases and 132 hospital-based controls consume fish once in a week.

The breast cancer cases that consumed 4 or more servings per week of fresh potatoes were 59 with 134 women observed in the hospital-based control group. Ninety-eight and 117 women consumed 2–3 servings per week of fresh potatoes (cooked) in the breast cancer cases and hospital-based control groups, respectively.

4–6 eggs and 1–3 eggs were consumed per week by 154 and 50 breast cancer cases respectively, while 225 and 49 women with the same consumption rate were observed in the hospital-based control group.

Table 2: The distribution of characteristics in the study population

Variables	Breast cancer patients	Hospital-based controls	Significant
Age (years)			
0–29	6	109	<0.05
30–39	41	67	
40–49	54	52	
50–59	93	48	
60–69	111	26	
Breast density			
Extremely dense	25	34	<0.05
Heterogeneously dense	179	129	
Almost entirely fatty	101	139	
Menopausal status			
Premenopausal	117	221	<0.05
Postmenopausal	188	81	
Age at menarche (years)			
≤12	73	6	<0.05
13	170	214	
14	62	82	

Table 3: The dietary consumption of the study population

Diets	Breast cancer patients	Hospital-based controls	Significant
Eggs			
4–6 per week	154	225	<0.05
1–3 per week	50	49	
None	101	28	
Fruits and vegetables			
5 or more servings per day	106	161	<0.05
3–4 servings per day	48	58	
2 servings per day	45	65	
None	106	18	
Olives and olive oil			
5 or more servings per day	41	49	<0.05
3–4 servings per day	52	86	
2 servings per day	115	150	
None	97	17	
Fish			
2 servings per week	83	160	<0.05
1 serving per week	119	132	
Never	103	10	
Fresh potatoes (cooked)			
4 or more servings per week	59	134	<0.05
2–3 servings per week	98	117	
1 or none per week	148	51	

A multivariable logistic regression model was used to analyze the food intake frequency, the least frequency of intake was used as the reference [Table 4]. The omnibus test of model, coefficients was significant ($P < 0.05$). Cox and Snell $R^2 = 0.442$ and Nagelkerke $R^2 = 0.590$. The Hosmer and Lemeshow test was also significant ($P < 0.05$). From the regression analysis, the intake of fruits and vegetables 5 or more servings/week and 2 servings/

Table 4: The logistic regression analysis of food intake frequency of the study group

Diets	B	Significant	OR	95% CI		P %
				Lower	Upper	
Fruits and vegetables						
Never (reference)		0.00	1.00			
5 or more servings/day	-2.4	0.00	0.09	0.04	0.18	7
3-4 servings/day	-2.3	0.00	0.10	0.04	0.20	9
2 times/day	-2.0	0.00	0.12	0.06	0.27	10
Eggs						
Never (reference)		0.00	1.00			
4-6/week	-2.2	0.00	0.10	0.05	0.20	9
1-3/week	-2.1	0.00	0.11	0.05	0.25	10
Olives and olive oil						
Never (reference)		0.00	1.00			
5 or more servings/day	-2.7	0.00	0.06	0.03	0.16	5
3-4 servings/day	-2.3	0.00	0.10	0.04	0.21	8
2 servings/day	-1.9	0.00	0.16	0.08	0.32	13
Fish						
Never (reference)		0.00	1.00			
2 servings/week	-3.1	0.00	0.04	0.02	0.10	3
1 serving/week	-2.7	0.00	0.06	0.03	0.15	5
Fresh potatoes (cooked)						
Never (reference)		0.00	1.00			
4 or more servings/week	-1.9	0.00	0.15	0.08	0.28	13
2-3 servings/week	-1.7	0.00	0.18	0.10	0.33	15

OR: Odds ratio, CI: Confidence interval

week had an odd ratio (OR) = 0.09 and 0.12, respectively. The OR = 0.10 and 0.11 was observed for the intake of 4-6 eggs/week and 1-3 eggs/week, respectively. Olives and olive oil intake 5 or more servings/week was 0.06, while the OR of 1 serving of fish/week was 0.06, Intake of 2 servings/week of fish OR = 0.04. Fresh potatoes 4 or more servings/week OR = 0.15.

The percentage probabilities (P) of breast cancer linked to each dietary category was calculated as $P = \frac{\text{Exp}(B)}{1 + \text{Exp}(B)} \times 100$ and is represented in Table 4.

DISCUSSIONS

Nutrition has long been suggested to impact breast cancer etiology in about 35% of disease cases,^[34] the sufficient consumption of foods containing essential nutrients is crucial to the modification of breast cancer risk in women.

The studied foods commonly consumed on the Mediterranean island of North Cyprus, which include, fresh potatoes, olives and olive oil, fruits and vegetables, eggs, and fish reduced the probability of breast cancer in all the women, proving that they are among the healthiest diets.^[35] Interestingly, Table 5 shows the first quartile the intake of fish 2 or 1 times per week followed by 5 or more times of olives and olive oil provided the highest protection in reducing the probability of breast cancer disease in women.

Table 5: Classification tables of odds ratio of dietary intake across quartiles

Quartiles	OR	95% CI	Dietary intakes
1 st	0.04	0.02-0.10	2 servings/week of fish
	0.06	0.03-0.15	1 serving/week of fish
	0.06	0.03-0.16	5 or more servings/day of olives and olive oil
2 nd	0.09	0.04-0.18	5 or more servings/day of fruits and vegetables
	0.10	0.04-0.21	3-4 servings/day of olive and olive oil
	0.10	0.04-0.21	3-4 servings/day vegetables and fruits
3 rd	0.10	0.05-0.20	4-6 eggs per week
	0.11	0.05-0.25	1-3 eggs per week
	0.12	0.06-0.27	2 servings/day of vegetables and fruits
4 th	0.15	0.08-0.28	4 or more servings/week of fresh potatoes
	0.16	0.08-0.32	2 servings/day of olives and olive oil
	0.18	0.10-0.33	2-3 servings per week of fresh potatoes

OR: Odds ratio, CI: Confidence interval

A case-control study situated in Italy with 2569 breast malignant growth cases and 2588 controls found an inverse relationship with fish intake, especially among postmenopausal women^[36] linked to the consumption of dietary marine n-3 polyunsaturated unsaturated fatty acids.^[37]

While an epidemiological and experimental proof recommended that olive oil may decrease the risk of specific tumors, specifically breast cancer,^[38] this may be due to the high monounsaturated fat content and concentration of poly-phenolic compounds in virgin and extra virgin olive oil.^[39]

1 These are the main wellspring of lipids within the customary
2 Mediterranean diet.^[29] According to studies, Mediterranean
3 dietary lipids have been shown to impact breast cancer.^[40]
4 These lipids play a significant role in the regulation of biological
5 activity and are important components of the cell membrane.^[41]
6 However, when the concentration of polyunsaturated lipids in
7 membranes is too high it may lead to an upsurge in fluidity and
8 peroxidation.^[42] Thus, moderate consumption of these lipids is
9 effective in decreasing oxidation damage in the membranes.^[43]
10 The protective effect of the intake of Mediterranean dietary lipids
11 on breast cancer may be through the signaling pathways such as
12 receptor tyrosine-protein kinase ErbB4-truncated protein, which
13 plays a part in mammary development and breast cancer and Ak
14 strain transforming pathway linked to apoptosis.^[44,45]

15
16 Mediterranean dietary lipids may decrease proliferation
17 through the down surge of epidermal growth factor-2
18 signaling pathway as Ki-67 has been shown to decrease
19 following the administration of lipids in malignant and
20 benign breast neoplasm.^[45-47] Dietary lipids influence the
21 decrease of factor-kB nuclear translocation and signaling
22 on peroxisome proliferation-activated gamma receptor and
23 through the interaction with the G-protein receptor 120,
24 which reduces apoptosis inhibitors and cytokines adhesion
25 molecules.^[48] Dietary lipids from Mediterranean foods are
26 shown to partially and beneficially affect the expression of
27 atherosclerosis-related genes,^[49] Tumor suppressor gene
28 p53 expression increased with the intake of fish-sourced
29 docosahexaenoic acid (DHA).^[50,51] Phenolic extracts from Brava
30 extra virgin olive oil minimized cell viability and induced
31 cell death in Michigan Cancer Foundation-7 breast cancer
32 cells.^[52] Breast cancer 1 and 2 genes also increased with
33 exposure of breast cells lines to omega-3 polyunsaturated
34 fatty acid (eicosapentaenoic acid and DHA) from fish.^[53] An
35 accompanied decrease in HER-2/neu an oncogene has been
36 seen in BT-474 and SKBr-3 breast cancer cells treated with oleic
37 acid supplements.^[54] Gago-Dominguez *et al.* observed a 30%
38 lower risk of breast cancer linked to glutathione-S-transferase
39 T1 null genotype in postmenopausal Chinese women living
40 in Singapore after the intake of marine dietary lipids from
41 fish.^[55] The benefits were more in postmenopausal women
42 with glutathione transferase (GST) polymorphisms that led
43 to low or no GSTT1, GSTP1, and GSTM1 activity.^[55]

44
45
46 To be able to recommend the right nutrition for a given
47 population, it is important to find the dietary intake that
48 incorporates all the nutrients required^[56] and when consumed
49 in the right amounts will provide optimum benefits.

50
51 The ability of a diet to provide prevention and reduction
52 of diseases that are linked to it determines its nutritional

1 sufficiency^[57] and genotype may be determining factor on how
2 these nutrients are made available for body use and function.
3 The frequency of polymorphism differs with ethnicity this
4 interplay needs to be studied to find out how breast cancer
5 can be modified by food intake in relation to genotype^[9] in this
6 population. Most societies especially the developing societies
7 can explore the advantages of Mediterranean diets through
8 research that looks for diets that are affordable, effective, and
9 locally available sources of sufficient micronutrients that can
10 reduce the risk of breast cancer.

11
12 The long-term control of breast cancer can be achieved when
13 the association between culture and nutritional selections
14 is considered when making policies because most societies
15 consider food as an essential part of their cultures, religious,
16 and social experiences.

17
18 Policies and programs that advocate home farms and gardens
19 can lead to the increased availability, affordability, and
20 consumption of healthy foods such as potatoes, vegetables,
21 fruits, eggs, fish, and olives in developing societies.

22
23 Also encouraging with incentives for people to set up
24 neighborhood supermarkets and eateries that sell these foods
25 will improve affordability and availability.

26
27 Agricultural subsidies in developing societies for producers
28 of these foods will encourage others to start producing thus
29 reducing cost and increasing availability.

30
31 Cultural festivals that promote and protect healthy foods are
32 important in sustaining healthy eating.

33
34 Civil society organizations, such as farming and fishing
35 cooperatives, religious groups, charitable organizations, and
36 women's groups, should play a part in public policy creation
37 and implementation.

38
39 Transnational food trade with proper regulations will enable
40 the availability of a variety of healthy foods coming from
41 across the borders.

42
43 Governments of developing societies that want to ensure
44 that nutritional objectives are adhered to in order to improve
45 the wellbeing of their citizens need to carry out school and
46 public education campaigns on diets and engage the food
47 and agriculture sectors.^[7] The awareness of the pivotal role
48 of these diets in breast cancer prevention will go a long way
49 in increasing the implementation of policies and programs
50 that target the right population.

Our study was carried out in a typical Mediterranean setting and reproducible. The cognitive impairment arising from illness and treatment may influence the answers provided by some breast cancer patients but to overcome this, patients were ensured to be in stable state by qualified medical practitioners before the interviews was conducted.

The case-control study method used has its limitations in the sense that the information collected is subject to recall bias. To minimize this a few food items were used in the food frequency questionnaire and the consumption categories were such that the participants could easily recall. However, such bias may not affect the results because the true effect may not be far from what was observed. The completeness of answers to the food items was used as a conformity test.

Despite the limitations considering that the dietary habits of the people of North Cyprus are similar to the traditional Mediterranean diets, an investigation of its effect on breast cancer risk is needed at the very moment because of the increase onset of the disease.

CONCLUSION

The Mediterranean diet has been shown to confer lots of health benefits and the intake of olives and olive oil 5 or more times daily, and fish 2 times weekly more significantly reduced the risk of breast cancer risk in the women of North Cyprus, the benefits of these foods can only be maximized when the appropriate policies that encourage the intake of healthy diet are established. The protection against breast cancer in comparison with other foods may be genotype related and calls for a need to study on a large scale the interplay between dietary intake in association with the genotype of this population.

Putting in perspective

Central question

1. What is the link between the intake of the Mediterranean diet and breast cancer prevention among the women of North Cyprus?

Key findings

1. The consumption of olives and olive oil 5 or more times, and fish 1 or 2 times weekly is significant in reducing the risk of breast cancer among the women of North Cyprus
2. There should be more awareness on the importance of the intake of the Mediterranean diets in breast cancer prevention.

Impact

1. The study will play a pivotal role in patient management and counseling on food intake
2. The study can be utilized in the creation of policies and programs that promote the production and consumption of healthy foods for the population of North Cyprus and other populations including the Indian population.

Further studies

1. There is a need for a larger study in the same population and other populations
2. The link between the dietary intake and the genotype of the population should be investigated.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

Healthy Lifestyle Profile Scale for Elderly: A novel tool to assess healthy lifestyle among young elderly live in South Asian settings

ABSTRACT

Background: Many lifestyle modification interventions have been introduced for young elderly population (aged from 60 to 74 years) in Sri Lanka to improve their health and well-being. However, little is known about the outcome of those interventions as there is no valid tool available to measure the level of a healthy lifestyle. This study was conducted to develop and validate a new tool to assess the level of healthy lifestyle among young elderly in Sri Lanka.

Materials and Methods: An operationalized definition of the healthy lifestyle was formulated. Items for the tool were identified following a literature review, key informant interviews, and focus group discussions. The content validity of the tool was ensured by the panel of experts. Both exploratory factor analysis (EFA) and confirmatory factor analysis (CFA) were conducted to explore factor structure and construct validity, respectively. The internal consistency, test-retest, and interobserver reliabilities of the tool were also assessed.

Results: Sixty-two items were identified initially, and they were reduced to 31 based on experts' opinion. Out of those, 28 items were loaded into 8 factors during the EFA. The results of the CFA showed a satisfactory model fit. Internal consistency (Cronbach's alpha >0.7), test-retest, and interobserver reliabilities (Interclass correlation coefficients >0.7) were also found to be satisfactory.

Conclusions: The tool was named the Healthy Lifestyle Profile Scale for Elderly (HLPSE). The HLPSE is a valid and reliable tool to assess the level of healthy lifestyle among Sri Lankan young elderly.

Keywords: Elderly, factor analysis, healthy lifestyle, reliability testing, Sri Lanka, validity

INTRODUCTION

A healthy lifestyle is a key determinant factor of health among elderly.^[1] A healthy lifestyle encompasses different dimensions such as physical activity, nutrition, mental relaxation, social relationships, and avoiding alcohol and smoking.^[2,3] Adherence to a healthy lifestyle improves the health-related quality of life and longevity among elderly. The construct of the healthy lifestyle has been introduced through different lifestyle modification interventions in different parts of the world and many of those showed positive results on elderly health.^[4,5] Similarly, lifestyle modification interventions have been implemented for elderly live in Sri Lanka and those are mainly targeted at young elderly (aged between 60 and 74 years) as they are more capable to adhere to healthy lifestyle instructions than old elderly (aged 75 years

and above). Those interventions are helpful in improving their health and wellbeing and provide better answers to health-related implications raised due to population aging

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of the country. However, little is known about the outcome of those interventions as there is no mechanism to measure the level of healthy lifestyle objectively.

There are many tools developed and utilized to assess the construct of healthy lifestyle in other parts of the world. Health Promoting Lifestyle Profile II^[6] and Health Protective Behavior Scale^[7] are such instruments that are used in the United States of America and China, respectively. Another instrument was developed and validated by Eshaghi in 2010 to assess healthy lifestyle among the Iranian elderly.^[8] Those tools were developed according to their sociocultural contexts thus, such tools may not be applicable to the Sri Lankan elderly who experience different sets of sociodemographic and cultural profiles. Furthermore, a similar kind of tool is not available in other South Asian countries which could be adjusted to Sri Lankan perspective. The unavailability of such measurement tools is a felt need to have a clear understanding of the level of healthy lifestyle among the Sri Lankan elderly. Therefore, the current study was conducted to develop and validate a new tool to assess the level of healthy lifestyle among young elderly population residing in Sri Lanka and other South Asian countries with similar sociocultural environments.

MATERIALS AND METHODS

Ethical approval was obtained from the Ethics Review Committee, Faculty of Medicine, University of Colombo. Informed written consents were obtained from all participants. The study population was young elderly people which has been defined as people aged between 60 and 74 years according to the local classification.^[9] The study was carried out in 7 phases.

Phase 1

In the first phase, the healthy lifestyle has been defined based on the consensus of experts in elderly health.

Phase 2 Item generation

In the second phase, items for the tool were generated based on conceptualized definitions following a literature search, key informant interviews, and focus group discussions.

Review of the literature

An extensive literature search was conducted using the following keywords: “Healthy Lifestyle,” “Health Promoting Lifestyle,” “Healthy Behaviors,” and “Tool AND Healthy Lifestyle.” Google Scholar and PubMed were used with the advanced search options. This was carried out to explore available tools and their items that could be used for the newly developed tool.

Key informant interviews

Key informant interviews were conducted among twelve stakeholders who were involved in elderly health at different levels. They represented different disciplines such as public health, behavioral science, sociology, psychology, and geriatric medicine. These were conducted to identify more appropriate items according to their expertise.

Focus group discussions

Four focus group discussions were conducted among young elderly living in urban and rural settings (two discussions per stratum) to accommodate their views and identify more country-specific items. All focus group discussions were audio recorded following informed written consent of the participants. Important items were identified after reviewing each recording carefully.

Phase 3

Content analysis of the items and preparation of scoring method

In the third phase, identified items were presented to the panel of experts using the Modified Delphi Technique. The expert panel consisted of a geriatric physician, a public health specialist, a sociologist, an university academic, and a health-promoting officer. However, experts who participated in the previous phase were excluded in this phase. All panel members were requested to rate each item from 1 to 10 based on cultural acceptability, clarity, and relevance separately. All responses were evaluated, and items that received higher scores were selected for the instrument, and they were transformed into questions and a response method was also formulated. The questionnaire was initially developed in English and then translated into Sinhala by bilingual experts. Each question could be rated on a 5-point Likert scale from 1 to 5. Participants were asked to respond to the questionnaire considering the past 2-week period from the time of data collection. Scores of each question were summated to determine the total score and it was transformed into a standardized score using the following formula.^[7] A higher score indicates a better level of healthy lifestyle.

Standardized score

$$= \frac{\text{Observed value} - \text{minimum value}}{\text{Maximum value} - \text{minimum value}} \times 100\%$$

Phase 4

In the 4th phase, the tentative questionnaire was pretested among 15 young elderly participants to explore the acceptability of the tool, and the questionnaire was adjusted according to the responses given by the participants.

Phase 5

Statistical item reduction

The draft questionnaire was subjected to exploratory factor analysis (EFA) during the 5th phase. A community-based cross-sectional study was conducted among 300 young elderly participants residing in the Kesbewa Divisional Secretary area in the Colombo district. Minimal sample size was calculated as nine participants per item in the tool.^[10] Participants who were already diagnosed to have psychiatric illnesses based on clinical records and were acutely ill at the time of the data collection were excluded from the study. The sample frame was prepared using the electorate list obtained from the Divisional Secretariate office Kesbewa. Participants were identified randomly using the prepared sample frame. Data collection was conducted by two trained field investigators who were trained simultaneously on the data collection procedure. In addition to the draft instrument, a judgmentally validated questionnaire was used to ascertain information related to the sociodemographic data. Both questionnaires were prepared as interviewers administered tools and field investigators collected data by visiting selected participants at their households. The collected data were entered into computer software (SPSS-23rd version) and analysis was performed.

Statistically significant results of Bartlett’s test of sphericity and the Kaiser–Meyer–Olkin (KMO) value higher than 0.6 were considered to decide sample adequacy.^[11] Eigenvalues of more than 1 were considered for factor loading^[12] and a Scree plot was also observed.^[13] Items were rotated using different methods to obtain the most meaningful factor structure. Identified factors were named appropriately while considering the contents of the items within a factor.

Phase 6

Construct validity of the instrument

In the 6th phase, the identified factor structure was subjected to confirmatory factor analysis (CFA) to ensure the construct validity of the tool.^[14] Another community-based cross-sectional study was conducted among a separate 280 young elderly people residing in a different setting to avoid contamination with participants in the previous phase. The same sample size calculation method and exclusion criteria used in phase 5 were adopted. Participants were recruited randomly using an electorate list of the Moratuwa Divisional Secretary area in the Colombo district. The collected data were analyzed using Lisrel 8.8. software. Absolute, relative, and parsimony fit indices were calculated and compared with acceptable values.

Phase 7

Reliability of the tool

Internal consistency, test–retest, and interobserver reliabilities were taken into consideration to evaluate the reliability of the tool during the 7th phase.

Internal consistency

The internal consistency was assessed by calculating Cronbach’s alpha coefficient for the total tool and each domain.^[15] Cronbach’s alpha coefficients equal to or above 0.7 were considered acceptable.^[16]

Test–retest reliability

The tool was re-administered among 30 randomly selected participants after 14 days from the initial date of data collection and interclass correlation coefficients (ICC) were calculated. The ICC value equal to or above 0.75 was considered good reliability.^[17]

Interobserver reliability

Since the tool was developed as an interviewer-administered one it was important to ensure interobserver reliability. Thus, the tool was re-administered to 20 randomly selected participants by another field investigator and total and domain-specific ICC values were calculated.

Table 1: Distribution of the sociodemographic characteristics of the participants in exploratory factor analysis (n=300)

Sociodemographic characteristic	Frequency (%)
Age category (years)	
60–64	76 (25.3)
65–69	112 (37.3)
70–74	112 (37.3)
Gender	
Male	113 (37.7)
Female	187 (62.3)
Ethnicity	
Sinhala	288 (96.0)
Non-Sinhala	12 (4.0)
Religion	
Buddhist	210 (70.0)
Non-Buddhist	90 (30.0)
Current marital status	
Currently married	198 (66.0)
Currently not married	102 (43.0)
Level of education	
Less than O/L	205 (68.3)
Equal or above O/L	95 (31.7)
Current employment status	
Currently employed	43 (14.3)
Currently unemployed	257 (85.7)
Income status	
Have a permanent monthly income	85 (28.3)
Not having a permanent monthly income	215 (71.7)

O/L: Ordinary level

RESULTS

The “Healthy Lifestyle for Young Elderly” was defined as “A set of actions and perceptions which will maintain and promote physical, mental, social and spiritual wellbeing of young elderly.” Initially, 62 items were identified during phase 2 and they were subjected to content analysis. Based on the consensus of the panel of experts, items were reduced to 31 and they were converted to questions. Those 31 questions were divided into actions and perceptions as denoted by the formulated definition and they were subjected to EFA.

Results of the exploratory factor analysis

Three hundred participants were interviewed out of selected 312, thus the nonrespondent rate was 3.8%. The mean (standard deviation [SD]) age of the participants was 66 years (SD = 2.8) and majority of them were

female (62.3%). Out of the total sample, 66% were married and 71.7% did not have a permanent monthly income [Table 1]. During the EFA, KMO value was found to be 0.709 and the value of Bartlett’s test of Sphericity was 2090.33 and it was statistically significant at a 0.0001 level. Thus, the study sample was adequate to perform factor analysis. Out of 31 initial items, three items showed multiple cross-loadings and they were removed from the tool. The remaining 28 items were loaded into 8 factors. The extracted eight factors were considered as domains of the tool and named appropriately as (1) physical activity, (2) mental health, (3) nutritional intake, (4) dietary concerns, (5) social relationships, (6) risk behaviors, (7) health responsibility, and (8) body consciousness [Table 2]. Those eight domains jointly explained 57.07% of the total observed variance. The newly developed tool has been named the Healthy Lifestyle Profile Scale for Elderly (HLPSE) and it is presented in Annexure 1.

Table 2: Domains and respective items with their loading coefficient

Domain number	Name of the domain	Item number	Item in the domain	Loading coefficient
1	Physical activity	1	How often you followed a planned exercise program	0.825
		4	How often you did walk for at least 30 min per day	0.807
		6	How often you did do activities to stretch your body	0.804
		10	How often you did do activities such as gardening, jogging, cycling, swimming, and dancing	0.666
2	Mental health	27	To what extent you would prefer walking or cycling instead of using a motor vehicle when traveling to nearby places	0.598
		3	How often you got enough sleep	0.591
		13	To what extent you felt relaxed in day-to-day life	0.665
3	Nutritional intake	18	To what extent you would like to engage with hobbies	0.432
		19	To what extent you could bear things in life that cannot be changed	0.696
		20	To what extent you viewed your life in a positive way	0.647
4	Dietary concerns	2	How often you ate at least 3 portions of vegetables per day	0.633
		5	How often you ate at least 2 portions of fruits per day	0.486
		8	How often have you consumed milk or milk product	0.751
5	Social relationships	9	How often you ate fish/meat/eggs	0.821
		17	To what extent you are concerned about consuming less sugar and sweet food items	0.632
		22	To what extent you are concerned about eating less oily food items	0.679
		23	To what extent you are concerned about eating less salty food items	0.766
6	Risk behaviors	24	To what extent you are concerned about drinking enough water	0.406
		14	To what extent you would like to discuss your problems with people close to you	0.402
		16	To what extent you would like to participate in common activities organized in your community	0.846
7	Health responsibilities	21	To what extent you would like to spend time with people close to you	0.848
		7	How often have you skipped your main meal	0.470
		11	How often have you consumed alcoholic beverages	0.722
8	Body consciousness	12	How often have you chewed beetle	0.746
		26	To what extent you could pay attention to health-related media programs or articles	0.433
		28	To what extent you would adhere to medical advice from a doctor	0.753
		15	To what extent you are concerned of your body weight	0.622
		25	To what extent you would like to discuss symptoms or changes in your body with a doctor	0.519

Results of the confirmatory factor analysis

The eight-factor tool was administered to 290 participants out of selected 300. Thus, the nonresponse rate was 3.3%. The mean age and SD of the participants were 63 and 2.3, respectively. Out of them, 65.2% were females and most of the participants (73.8%) were married at the time of data collection. The sociodemographic characteristics of the participants are shown in Table 3. During the CFA the calculated values of all three types of fit indices were compared with accepted cutoff values as shown in Table 4. According to the results, the 8-factor structure of the HLPSE showed a satisfactory model fit.

Results of the reliability of the Healthy Lifestyle Profile Scale for Elderly

The Cronbach's alpha coefficient for the total tool was 0.772 and it ranged from 0.687 to 0.837 across the eight domains. The calculated ICC values for test-retest and interobserver reliabilities were above 0.94 and 0.91, respectively, and the reliability results of HLPSE are shown in Table 5.

DISCUSSION

The construct of healthy lifestyle has been discussed in the literature for many years and several studies have been carried out to investigate how to measure it in many countries.^[6-8] Researchers have emphasized the significance of developing context-specific instruments to assess healthy lifestyle while putting more attention on given socio-cultural determinants.^[18,19] In Sri Lanka, many lifestyle modification programs are targeted at young elderly but the unavailability of a valid and reliable tool to measure healthy lifestyle was a felt gap. Considering the requirements of the country, this study was conducted to develop and validate a tool to measure the healthy lifestyle objectively among the young elderly population residing in Sri Lanka.

An operational definition for the healthy lifestyle was made initially after going through literature and based on the consensus of local experts and the tool has been conceptualized on the developed definition. The definition enabled to accommodate many items from different facets of the healthy lifestyle of young elderly. The items for the present tool were identified following qualitative assessments and a literature review which also facilitated to capture of different aspects of the construct to be measured and more importantly gathering specific information relevant to the Sri Lankan context. A similar methodology was used by other researchers while developing tools relevant to their context.^[18] All selected items were evaluated by local experts, which enabled the recruitment of more relevant items for the newly developed HLPSE.

Table 3: Distribution of the sociodemographic characteristics of the participants in confirmatory factor analysis (n=290)

Sociodemographic characteristic	Frequency (%)
Age category (years)	
60–64	88 (30.3)
65–69	111 (38.3)
70–74	91 (31.4)
Gender	
Male	101 (34.8)
Female	189 (65.2)
Ethnicity	
Sinhala	283 (97.6)
Non-Sinhala	7 (2.4)
Religion	
Buddhist	216 (74.5)
Non-Buddhist	74 (25.5)
Current marital status	
Currently married	214 (73.8)
Not currently married	76 (26.2)
Level of education	
Less than O/L	203 (70.0)
Equal or above O/L	87 (30.0)
Current employment status	
Currently employed	44 (15.2)
Currently unemployed	246 (84.8)
Income status	
Have permanent monthly income	94 (32.4)
Not having a permanent monthly income	196 (67.6)
Chronic diseases status	
Presence of chronic diseases	259 (89.3)
Absence of chronic disease	31 (10.7)

O/L: Ordinary level

Table 4: The goodness of fit indices of the Healthy Lifestyle Profile Scale for Elderly in comparison to accepted model fit indices

Fit indices	Values of the HLPSE	Accepted values	Reference
Absolute fit indices			
χ^2/DF	1.51	<3	[23]
SRMR	0.059	<0.08	[13]
Goodness of fit index	0.89	>0.9	[13]
Parsimony fit index			
RMSEA	0.042	<0.08	[24]
Relative fit indices			
Comparative fit index	0.95	>0.9	[25]
Incremental fit indices	0.95	>0.9	[26]
Nonnormed fit index	0.94	>0.9	[25]
Normed fit index	0.87	>0.9	[13]

DF: Degree of freedom, SRMR: Standardized root mean square residual, RMSEA: Root mean square error of approximation, HLPSE: Healthy Lifestyle Profile Scale for Elderly

Items of the HLPSE are divided into actions and perceptions which is the unique feature of the tool when compared to other similar measurement tools. It is very important to consider both aspects when taking measurements to enhance the health and well-being of the study population. However,

Table 5: The results of the reliability assessment of the Healthy Lifestyle Profile Scale

Name of the domain	Cronbach's alpha	Test-retest reliability		Interobserver reliability	
		ICC value	95% CI	ICC value	95% CI
Overall HLPSE	0.772	0.94	0.87–0.97	0.91	0.84–0.97
Physical activity	0.815	0.94	0.88–0.97	0.99	0.97–0.99
Mental health	0.756	0.84	0.68–0.93	0.88	0.69–0.95
Nutritional intake	0.711	0.93	0.85–0.97	0.92	0.79–0.97
Dietary concerns	0.733	0.88	0.76–0.94	0.91	0.78–0.97
Social relationships	0.687	0.86	0.71–0.93	0.94	0.87–0.98
Risk behaviors	0.772	0.98	0.95–0.99	0.97	0.94–0.99
Health responsibilities	0.837	0.81	0.59–0.91	0.95	0.88–0.98
Body consciousness	0.819	0.89	0.77–0.95	0.84	0.59–0.94

CI: Confident interval, HLPSE: Healthy Lifestyle Profile Scale, ICC: Interclass correlation coefficient

in many similar tools, it was not possible to differentiate actions from perceptions and thus cannot be analyzed separately. In contrast to other tools, HLPSE gives the added advantage of an understanding of the two components separately thus permitting the planning of new interventions appropriately in the future.

HLPSE consists of eight domains that are consistent with the domains identified in other similar tools.^[6,8,18] Furthermore, the identified domains were consistent with the theoretical foundation and defined construct of the healthy lifestyle for young elderly. These eight domains explained about 57% of the cumulative variance which is similar to variances explained by other tools made to measure the same construct.^[18,20] Out of the total variance, the majority was explained by the physical activity domain that indicating the significance of it in relation to healthy lifestyle among Sri Lankan young elderly. A similar pattern was identified by Hwang and Peralta-Catipon as physical activity is the major contributory factor in the Health Enhancing Lifestyle Profile tool.^[21] However, in contrast to other instruments, in the HLPSE, items related to consuming good food are distinct from items of avoiding unhealthy food and were loaded separately to form two domains as nutritional intake and dietary concerns respectively. This shows that two components of diet and nutrition, which have been classified as a single domain in other tools, were seen differently by the Sri Lankan young elderly.

CFA was conducted as a way of ensuring the construct validity of the HLPSE and the same method was used by other researchers while developing their tool.^[22] The identified eight-factor structure was found to have a good model fit as evidenced by the results. Internal consistency is a measurement of the reliability of a composite tool that assesses the extent to which all items measure the same construct.^[23] The study showed an acceptable Cronbach's alpha value for all domains except social relationships. Somewhat

lower Cronbach's alpha for the social relationship domain might be explained by certain behavioral characteristics of the Sri Lankan young elderly associated with that dimension.

The HLPSE demonstrated good test–retest reliability which indicates the consistency of the measurements over time. Interobserver reliability is a more important measurement for the new scale since it has been developed as an interviewer-administered tool. The values of ICC in the overall scale and individual domains were well above the expected cutoff of 0.75^[17] which ensured the consistency of the measurements between investigators and also helped to eliminate interviewers' bias. Since the tool is developed as an interviewer-administered scale it is convenient to use even among the illiterate and less educated population. In the absence of a gold standard scale, it was not possible to assess the criterion validity of the tool which has been identified as a limitation of this study.

CONCLUSIONS

The HLPSE is a valid and reliable tool to assess the construct of healthy lifestyle among young elderly in Sri Lanka. It is suggested to validate the tool in other South Asian settings where similar socio-cultural profiles are observed. Thus, the tool could be applicable to assess healthy lifestyle among elderly and effectiveness of the lifestyle interventions in future.

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Conflicts of interest

There are no conflicts of interest.

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Annexure

AQ2 Annexure 1: Questionnaire to assess healthy lifestyle profile among young elderly (aged 60 to 70 years)

Questionnaire to assess Healthy Lifestyle Profile (HLP) among young elderly (Aged 60 to 74 years)

The following questions are about actions and perceptions related to your present way of life. The questionnaire consists of two parts. The part A consists of questions related to your actions and part B consists of questions related to your perceptions. Each question and relevant response will be read separately for you. Please think about the last 2 weeks period and give the most appropriate answers. Please try not to skip any questions.

Part A

The following questions are about actions related to your lifestyle. Please respond to each question separately based on how often you engaged with each action during the last 2 weeks. Please respond as follows:

- 1 = Never (Did not engage during last 2 weeks)
- 2 = Rarely (1 or 2 days during last 2 weeks)
- 3 = Sometime (3 to 5 days during last 2 weeks)
- 4 = Often (6 to 9 days during last 2 weeks)
- 5 = Very often (10 or more days during last 2 weeks)

Example:

How often you engaged in exercises?

Never	Rarely	Sometimes	Often	Very often
1	2	3	4	5

If you engaged with 10 or more days during last 2-weeks, give your response as "5"

1. How often you followed a planned exercise program?

- Never 1
- Rarely 2
- Some times 3
- Often 4
- Very often 5

2. How often you ate at least 3 types of vegetables per day?

- Never 1
- Rarely 2
- Some times 3
- Often 4
- Very often 5

3. How often you got enough sleep?

- Never 1
- Rarely 2
- Some times 3
- Often 4
- Very often 5

4. How often you did continuous walking at least 30 min per day?

Never	Rarely	Some times	Often	Very often
1	2	3	4	5

5. How often you ate at least 2 types of fruits per day?

Never	Rarely	Some times	Often	Very often
1	2	3	4	5

6. How often you did activities to stretch your body?

Never	Rarely	Some times	Often	Very often
1	2	3	4	5

7. How often you skipped your main meal?

Never	Rarely	Some times	Often	Very often
5	4	3	2	1

8. How often you consumed milk or milk product?

Never	Rarely	Some times	Often	Very often
1	2	3	4	5

9. How often you ate fish/ meat/eggs?

Never	Rarely	Some times	Often	Very often
1	2	3	4	5

10. How often you did activities such as brisk walking, cycling, running, swimming, dancing?

Never	Rarely	Some times	Often	Very often
1	2	3	4	5

11. How often you consumed alcoholic beverages?

Never	Rarely	Some times	Often	Very often
5	4	3	2	1

12. How often you chewed betel?

Never	Rarely	Some times	Often	Very often
5	4	3	2	1

Part B

The questions in this part are about your perceptions related to your lifestyle. Please think about last 2 weeks and respond each question based on to what extent they related to you. Please respond as follows:

Example –

To what extent are you concerned about your health?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

If you feel you are concerned about your health to some extent, give your response as “3”

13. To what extent you felt relaxed in day to day life?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

14. To what extent you would like to discuss your problems with people close to you?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

15. To what extent you are concerned of your body weight?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

16. To what extent you would like to participate in common activities organized in your community?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

17. To what extent you are concerned about consuming less sugar and sweet food items?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

18. To what extent you would like to engage with hobbies?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

19. To what extent you could bear things in life that cannot be changed?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

20. To what extent you viewed your life in a positive way?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

21. To what extent you would like to spent time with people close to you?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

22. To what extent you are concerned about eating less oily food items?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

23. To what extent you are concerned about eating less salty food items?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

24. To what extent you are concerned about drinking enough water?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

25. To what extent you are concerned of changes of your body?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

26. To what extent you could pay attention to health-related media programs or articles?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

27. To what extent you would prefer walking or cycling instead of using motor vehicle when traveling to nearby places?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

28. To what extent you would adhere to medical advices from a doctor?

Not at all	To little extend	To some extent	To more extent	To great extent
1	2	3	4	5

Case Report

Ostial left anterior descending artery chronic total occlusion – Left main coronary artery intramural hematoma

ABSTRACT

Chronic total occlusion (CTO) intervention of ostial left anterior descending artery lesion without clear cap poses challenges for wiring. Intravascular ultrasound-guided antegrade cap puncture and guide extension-assisted reverse-controlled antegrade and retrograde tracking away from the ostium would minimize inflow injuries. This case report explores inflow injury and its detection by imaging in ostial left anterior descending artery CTO percutaneous coronary interventions.

Keywords: Ambiguous cap puncture, flap closure, intramural hematoma, reverse-controlled antegrade and retrograde tracking

INTRODUCTION

Chronic total occlusion (CTO) intervention of ostial left anterior descending artery (LAD)/left circumflex artery (LCX) lesions without a clear cap poses challenges for wiring due to the angle of entry and unclear entry. Ostial LAD CTO, by being in a location supplying a significant portion of the myocardium, increases the risk of percutaneous coronary intervention (PCI) due to inflow injuries such as left main coronary artery (LMCA) dissections or intramural hematoma (IMH).^[1] In one of the large-scale analyses of ostial LAD CTO PCI in 13 centers in Korea, it was observed that the cap is ambiguous in 43% of cases and apparent dissections requiring rescue procedures were noted in 5.2% of cases.^[2] Ostial LAD CTO is a different animal to tame due to the special operator attention needed to prevent intraprocedural catastrophes such as dissection or IMH of LMCA or LCX.^[3] Intravascular ultrasound (IVUS)-guided cap puncture followed by using this wire position for antegrade preparation to receive the retrograde wire beyond the ostium of LAD minimizes aforementioned complications and makes the procedure

as predictable as possible.^[4] We report a case of ostial LAD CTO intervention, in which LMCA IMH complicated the stenting strategy.

CASE REPORT

We report a 60-year-old male hypertensive, diabetic treated for acute ST elevation inferior wall myocardial infarction (IWM) with primary angioplasty with stent to the mid-right coronary artery [Figure 1a-c].

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He was admitted for ostial LAD CTO PCI. As the proximal cap was not clear, IVUS-guided antegrade cap puncture was planned, followed by retrograde if needed. IVUS-guided antegrade cap puncture was done using a double-lumen catheter (Crusade, Kaneka Corporation, Japan) and IVUS catheter (OptiCross, Boston Scientific) on the same workhorse wire through an 8 FR guide [Figure 2a]. Initial cap puncture with Hornet 10 (Boston Scientific) was subintimal [Figure 2b]; however, in subsequent attempts, the wire could be navigated into the proximal cap successfully [Figure 2c]. Workhorse wire on which OptiCross was positioned into LCX was pulled back till the tip of the wire was out of the IVUS catheter monorail exit. Then, the IVUS catheter was withdrawn [Video 1a and b], followed by double-lumen catheter exchanged to corsair XS (Asahi

Intecc) [Figure 2d] on LAD wire into and beyond the ostium of LAD to consolidate the position achieved.

Antegrade wire de-escalated to GAIA II (Asahi Intecc) and advanced further but halted because of the ambiguous vessel course in retrograde injection. Retrograde wiring through septal collateral was done with caravel 150 mm (Asahi Intecc) through the guide extension in a 7 FR JR guide. After caravel positioned into LAD contrast injection done to delineate the course of LAD for further wiring [Video 2a]. To our surprise, contrast injection created subintimal dissection with retrograde extension to ostial LAD. Conventional reverse cart [Video 2b] with 3.5 × 12 mm balloon over GAIA II in the ostial LAD and Hornet 10 retrograde wire was done successfully, followed by confirmation of intimal

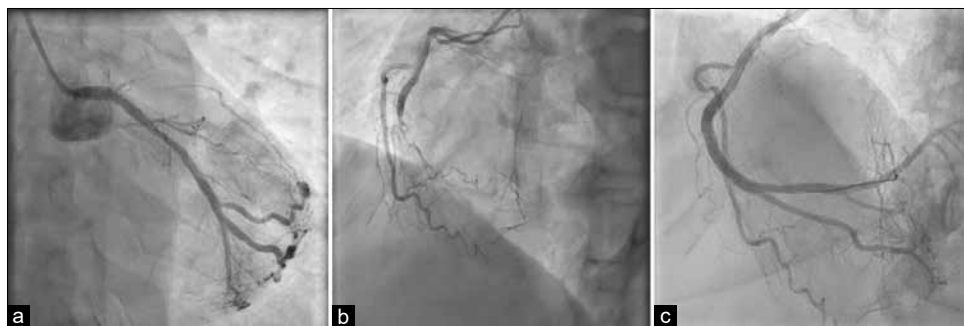


Figure 1: (a) Right coronary artery (RCA) angiogram before primary percutaneous coronary interventions (PCI) - Total thrombotic occlusion of mid-RCA, (b) Left system - ostial left anterior descending artery chronic total occlusion with mild left circumflex artery disease, (c) Post primary PCI to RCA - Dominant RCA with normal distal branches

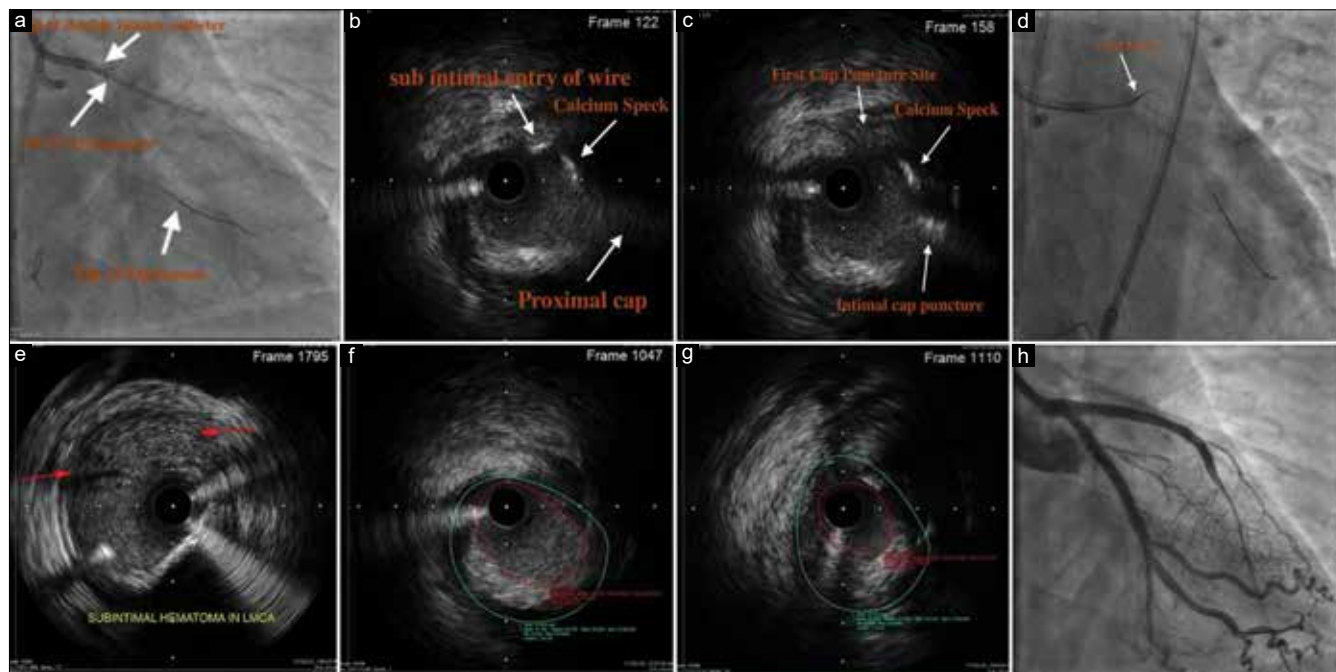


Figure 2: (a) Intravascular ultrasound (IVUS)-guided cap puncture - IVUS catheter, (b) IVUS showing antegrade wire entry at subintimal plane away from cap, (c) IVUS - Hornet 10 in proximal cap, (d) Fluro-Hornet 10 in proximal cap, (e) IVUS - Intramural hematoma compressing true lumen, (f) Ostial left circumflex artery (LCX) minimum lumen area (MLA) in IVUS before LM TO left anterior descending artery (LAD) stent (MLA: 5–6 mm²), (g) Ostial LCX MLA after left main coronary artery to LAD stent followed by POT (MLA: 2–3 mm²), (h) Final angiogram result

wire entry from LAD into LMCA by IVUS [Video 2c]. After externalization, predilatation of the lesion was performed, followed by antegrade wiring of distal LAD through the double-lumen catheter on the externalized wire. Retrograde wire is removed, followed by IVUS imaging done from LAD for stenting strategy. IVUS revealed IMH [Figure 2e] extending into distal LMCA. Stenting was done from ostial LMCA into LAD with 2.75 mm × 38 mm and 3.5 mm × 28 mm stent with overlap at no branch zone of proximal LAD. After POT for LMCA and optimization of LAD stent by post dilatation, IVUS from LCX revealed a minimum lumen area of 2.3 mm² against the baseline of 5.6 mm² [Figure 2f and g]. TAP stenting was done with 3.0 mm × 28 mm stent into LCX, followed by bifurcation optimization [Figure 2h].

DISCUSSION

Ostial LAD CTO poses challenges due to the abnormal angle of attack with the antegrade wire. Furthermore, the presence of ambiguous cap, seen in 43.3% of cases in Korean data, amplifies the technical challenges for antegrade wiring.^[2] Figure 3a-c illustrates the ideal wiring strategy for ostial LAD CTO with ambiguous cap to minimize inflow injury.

Indeed, the same Korean study showed a 5.2% incidence of inflow dissections requiring stenting of LMCA or LCX². Understandably, inflow vessel injury/dissection was more frequent in patients with LMCA disease or ambiguous proximal cap. The presence of both anatomic factors would have an additive impact on the incidence of dissection. Other factors in antegrade wiring which might affect inflow injury are angle of attack, type and shape of the wire used, type of microcatheter, and use of imaging. Higher angle of attack, ambiguous cap puncture without imaging guidance, and cap puncture with microcatheter positioned away from the proximal cap increase the incidence of dissection.^[5] Double-lumen catheter with live IVUS would increase the accuracy of targeted cap puncture with lesser chances of inflow injury. Antegrade preparation with complete

IVUS-guided cap puncture is considered the Achilles heel of ostial LAD CTO.^[3] After antegrade cap puncture under IVUS, the wire position achieved must be consolidated by advancing the microcatheter into and beyond the ostial LAD. In the event of failure of antegrade wire reaching the distal true lumen, parallel wire with the double-lumen catheter positioned into the LAD in such a way that the second wire also goes through the same ostial LAD entry can be done or switch to retrograde wiring. When retrograde wiring is used reverse-controlled antegrade and retrograde tracking (CART) should be performed beyond the ostial LAD, preferably, with guide extension assistance to make sure retrograde wire enters LMCA through the antegrade entry created under IVUS. Caution should be taken to stay distal and away from LAD ostium with retrograde wire during reverse CART. Directed reverse CART with retrograde wire directed onto the distal tip of antegrade balloon would minimize the proximal LAD injury in the presence of shorter length of antegrade space created. If guide extension cannot be used, intimal entry of retrograde wire into LMCA should be confirmed by IVUS before externalization. In situations of retrograde wiring without antegrade preparation, retrograde wire navigation into LMCA must be done under IVUS for ideal entry into LMCA without creating inflow injury. In a rare situation, when a high tip-load guidewire is needed to puncture the proximal cap retrogradely but is less controllable (either by poor microcatheter support or severe vessel angulation), elective stenting from the LMCA to the LCX may facilitate direct wiring while ensuring the safety. However, this strategy should be justified by other indications for LMCA-LCX stenting, such as the presence of LMCA disease or ostial LCX disease.^[2] Inflow injury is mostly noticed after CTO wiring but sometimes can be seen after predilatation of ostial LAD. Therefore, LMCA anatomy must be analyzed carefully by IVUS from LAD and/or LCX after the lesion preparation before embarking on the stenting strategy. Any inflow dissection or IMH extension into LMCA warrant's two-stent strategy. Consider placing LMCA stent from the ostium to avoid proximal lumen compromise by IMH shift.

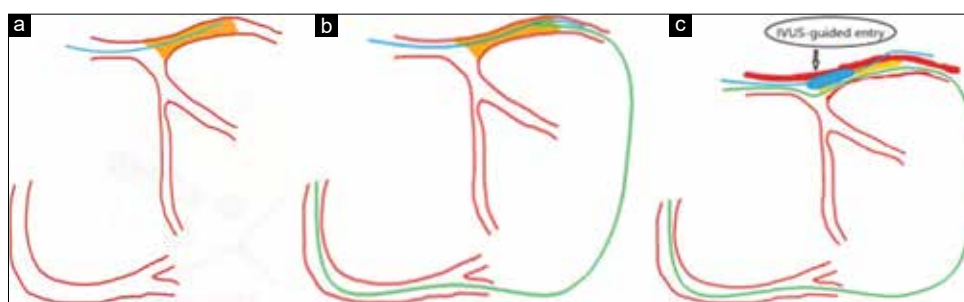


Figure 3: Steps for ostial left anterior descending artery chronic total occlusion percutaneous coronary interventions with ambiguous cap. (a) Step 1 - Intravascular ultrasound-guided cap puncture, (b) Step 2 - Going retrograde, (c) Step 3 - Reverse-controlled antegrade and retrograde tracking, beyond the ostium with guide extension

CONCLUSION

Ostial LAD CTO PCI constitutes a special subset due to the larger area of the myocardium at risk. Careful wiring both antegrade and retrograde to prevent inflow injuries and meticulous analysis of LMCA anatomy in IVUS to identify inflow injuries before embarking on stenting strategy are quintessential to prevent catastrophe.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Learning objectives

- Approach to ostial LAD CTO needs special attention to avoid on-table catastrophe
- IVUS-guided antegrade cap puncture is essential, which also acts as an antegrade preparation for retrograde
- Guide extension-assisted reverse CART would ensure favorable retrograde wire entry
- Stenting strategy needs to be dynamic and decide based on the IVUS appearance of distal LMCA after reverse cart.

- IMH in LM in IVUS stenting from LM ostium is a safer strategy
- Always re-assess ostial LCX in IMH scenarios after LMCA to LAD stenting.

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Conflicts of interest

There are no conflicts of interest.

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Case Report

Severe resistant trigeminal neuralgia managed successfully by computed tomography-guided gasserian ganglion block

ABSTRACT

The present case report discussed the management of a 62-year-old female patient with medically refractory trigeminal neuralgia (TN) with percutaneous computed tomography-guided gasserian ganglion block (CT-GGB). Using Hartel anterior approach, we successfully performed CT-GGB with precise positioning of the 22G LP needle tip in the medial aspect of the foramen ovale at the base of the skull as was witnessed clinically by the patient as sharp pain along the affected areas of the face, confirmed by serial CT screening until it reaches the predefined depth. Later, neurolysis mixture was injected, and the needle was finally flushed with 0.5 ml of normal saline and then withdrawn. Sterile dressing was applied at the skin entry site after removing the LP needle. Postprocedural check, CT was performed to look for any immediate complications. Patients were observed for regular follow-up at 1 week, 2 weeks, 1 month, 3 months, and every 3 months after that. The patient was relieved entirely of facial pain on the CT table (Numerical Rating Scale Pain Score-0) with minimal facial numbness and no sensation loss. To conclude, CT-GGB invention is an effective and safe technique for medically refractory TN.

Keywords: Computed tomography, gasserian ganglion block, neurolysis mixture, trigeminal neuralgia

INTRODUCTION

Trigeminal neuralgia (TN) is a painful condition that causes shooting or jabbing sensations similar to an electric shock on one side of the face and is more likely to occur in people older than 50 years, affecting women more often than men. The symptoms may be short-lived mild attacks but can progress to more frequent chronic bouts of searing pain involving the trigeminal nerve, which carries sensation from face to brain. Although the condition is not life-threatening, the intensity of the pain can be debilitating. Treatment options range from medications to surgical (microvascular decompression) management. Percutaneous rhizotomy procedures (balloon compression, glycerol injection, and radiofrequency thermal lesioning) are on the rise; however, they are performed using fluoroguidance with little literature on computed tomography (CT) use as a tool of interest.

CASE REPORT

A 62-year-old female came to the interventional radiology department with a history of chronic toothache which had undergone root canal management, complaining of

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right-sided severe facial pain diagnosed as TN and was on medical management. At present, she suffers from severe pain in the right half of her face with mild swelling, which worsens while brushing, eating, chewing, and swallowing. She has been unable to sleep for the last 3 days owing to severe sharp pain. She is a known diabetic, hypertensive, hypothyroid, seizure disorder, multi-infarct state and was admitted to the hospital with altered sensorium twice in a span of the last 3 months, during which she was found to have hypoglycemic encephalopathy, septic shock on first admission, and hypomagnesemia on second admission for which she was treated conservatively and recovered completely. Her magnetic resonance imaging (MRI) brain plain revealed multiple chronic lacunar infarcts in bilateral thalami, left caudate nucleus, both halves of the midbrain, and right cerebellum with mild-to-moderate periventricular and subcortical ischemic changes in bilateral frontal and parietal regions. Three-dimensional FIESTA MRI did not reveal any significant abnormality [Figure 1]. The treating team converged on a diagnosis of TN resistant to conservative medical management and offered her options of surgical management and percutaneous CT-guided gasserian ganglion block (GGB). After understanding its risks and benefits, the patient and their relatives opted for a CT-guided procedure. Basic preprocedural blood investigations were done, perioperative antibiotics started, and Numerical Rating Scale Pain Score (NRSP) was recorded. The patient was placed in a supine position with headfirst (toward the gantry) on the CT table with neck extended and head tilt of 15°–30° contralateral to the affected side of the face. Sterile draping and local anesthetic infiltration at the skin entry site were done. Using Hartel anterior approach, we successfully performed CT-guided percutaneous-GGB with precise positioning of 22G lumbar puncture (LP) needle tip in the medial aspect of the foramen ovale at the base of the skull as was witnessed by a patient

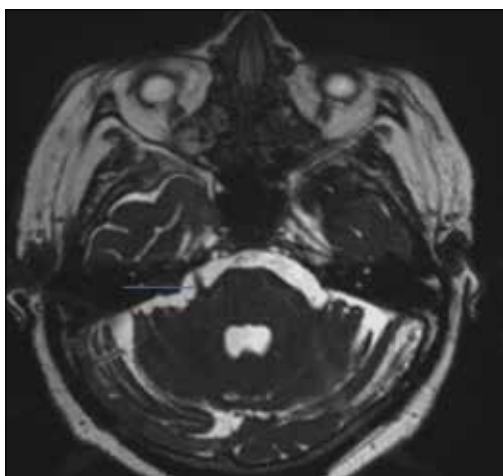


Figure 1: Magnetic resonance imaging brain three-dimensional FIESTA showing right trigeminal nerve (blue arrow)

as sharp pain along the affected areas of the face, confirmed by serial CT screening until it reaches the predefined depth. Following this neurolysis, mixture consisting of 1 ml (40 mg) triamcinolone, 2 ml of 2% xylocaine, 3 ml of 0.5% bupivacaine, and 0.5 ml contrast were injected [Figures 2-4]. The needle was finally flushed with 0.5 ml of normal saline and then withdrawn. Sterile dressing was applied at the skin entry site after removing the LP needle. Postprocedure check CT was performed to look for any immediate complications. The patient was observed for 2 h and then sent home with advice to monitor blood sugars, stop oral analgesic medications, and regular follow-up at 1 week, 2 weeks, 1 month, 3 months, and every 3 months after that.

RESULTS

The patient was relieved entirely of facial pain on the CT table (NRSP-0) with minimal facial numbness and no sensation loss. There were no immediate procedure-related complications; swelling of the cheek increased at 1-month follow-up (NRSP-2) with a gradual reduction at 3-month follow-up (NRSP-0). Her overall quality of life has improved, and she can do her day-to-day activities efficiently even at 1-year follow-up posttreatment.

DISCUSSION

“TN is defined by paroxysmal, sudden, unilateral, brief, electric shock-like, and recurrent pain in the facial region innervated by the trigeminal nerve.” Refractory TN can lower a patient’s quality of life and cause depression.^[1] Antiepileptic medications are used as the first line of treatment for TN, although they are unsuccessful in some patients, and some patients cannot tolerate their adverse effects. Despite the availability of other surgical procedures, a nerve block is a quick and secure percutaneous therapy for TN patients. In the present case report, we reported a case complaining of right-sided severe facial pain diagnosed as TN and subjected to a CT-guided percutaneous-GGB

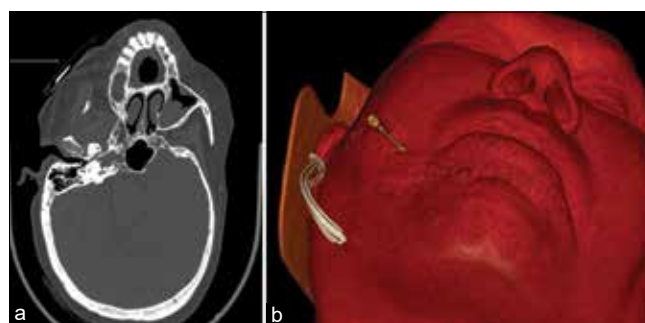


Figure 2: Computed tomography axial view (a) and three-dimensional volume-rendered reformat (b) showing dense radio marker (blue arrow); lateral head tilt positioning along with the site of needle entry

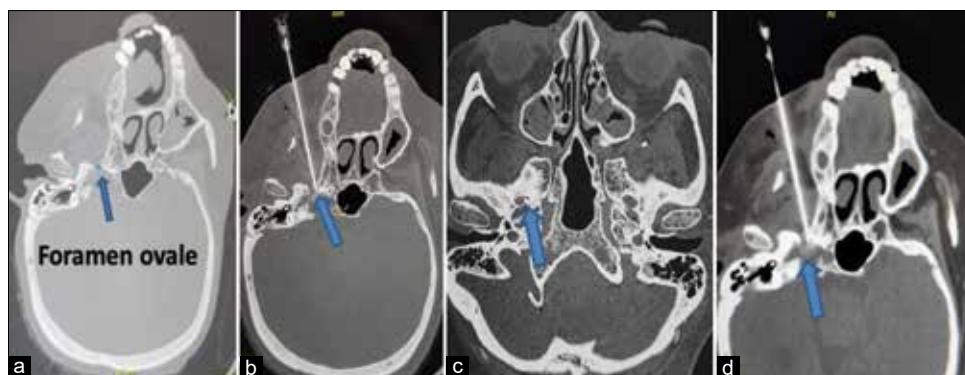


Figure 3: Computed tomography brain sections with blue arrows showing (a) foramen ovale, intra-procedure: needle tip (b and c) in the medical aspect of foramen ovale with drug percolation (d)

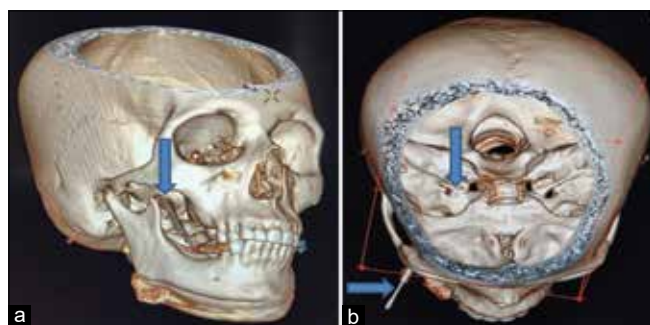


Figure 4: Three-dimensional volume-rendered images (a and b) of the skull showing the needle entry point and its tip within foramen ovale (blue arrows)

procedure. She was completely relieved of facial pain on the CT table (NRSP-0) with minimal facial numbness and no sensation loss. There were no immediate procedure-related complications; swelling of the cheek increased at 1-month follow-up (NRSP-2) with a gradual reduction at 3-month follow-up (NRSP-0). Her overall quality of life has improved, and she can do her day-to-day activities efficiently even at 1-year posttreatment. According to the authors literature review, only two studies were pertinent to the current investigation. In a prospective study by Lan *et al.*,^[2] involving 28 patients with idiopathic TN who underwent CT-guided percutaneous pulsed radiofrequency treatment of the gasserian ganglion, the researchers discovered that the postoperative Numerical Rating Scale (NRS) score steadily reduced from 7.6 preoperative to 0.1 postoperative. Recently, Sun *et al.*,^[3] conducted a multicentric retrospective analysis on patients who had received a gasserian ganglion block with CT guidance and suffered from acute or subacute zoster-related TN. According to their research, all patients postoperative NRS scores considerably dropped. At various time points, the acute zoster group's NRS scores were lower than those of the subacute zoster group. The current case uses a local anesthetic and steroid combination as neurolysis mixture for refractory TN. Medically unresponsive TN can be treated safely and effectively with CT-guided innovation.

CONCLUSION

In clinical scenarios with comorbidities, as discussed above, minimally invasive percutaneous interventional procedures such as CT-guided GGB can relieve severe facial pain with a low risk of complications. CT guidance during the procedure ensures better accuracy, safety, and favorable response in pain relief. However, future studies must be investigated to determine the ultimate effective and safer choice.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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AQ5: Please provide revised date

AQ6: Kindly provide the expansion.

AQ7: Based on the information available in FP document that consent form has been obtained from all patients we have included the declaration statement. Please confirm whether it is needed or not.

Case Report

A rare case of rectal perforation in high anorectal malformations

ABSTRACT

Spontaneous perforation is a rare complication in anorectal malformation. The colon is the most common site of perforation in anorectal malformations.^[1] The median age of perforation is 48 h 1. Here, we report a case of a newborn male with high anorectal malformation with perforation in the blind pouch of the rectum at 18 h of life.

Keywords: Anorectal malformation, colostomy, neonates, pneumoperitoneum

INTRODUCTION

The incidence of spontaneous perforation in a newborn with anorectal malformation is 2%–9.5%.^[2] The most common site of perforation is the colon.^[3] The aim of this case report is to emphasize that early detection of complications (pneumoperitoneum) reduces morbidity and mortality.

CASE REPORT

A term male baby delivered by emergency LSCS in view of nonprogression of labor was admitted to the neonatal intensive care unit (NICU) in view of the absent anal opening. All the antenatal scans were normal, with no maternal comorbidities. Perineal examination revealed an absent anal opening. The baby was shifted to tertiary care NICU at 2 h of life in view of the above diagnosis. In view of the major congenital anomaly, two-dimensional ECHO was done, which was normal. Ultrasonography abdomen was suggestive of nonvisualization of the left kidney. Serial X-rays of the abdomen and pelvis in erect posture were taken every 6 h to see the descent of gas shadow. An X-ray at 8 h of life showed the descent of gas shadow till the ileal region. At this point, the plan was to monitor for further descent of gas shadow. At 18 h of life baby had sudden abdominal distension with visible veins in anterior abdominal wall. Bowel sounds

were not heard. X-ray of erect abdomen suggestive of pneumoperitoneum [Figure 1].

The baby was taken for emergency laparotomy after initial resuscitation with written informed consent. Operative findings: A small perforation of approximately 5 mm was seen in the most dependent part of the distal blind ending rectal pouch [Figure 2]. The perforation was closed using Vicryl - 5.0, interrupted sutures with a protective left pelvic colostomy [Figure 3]. Postsurgery, the baby was kept on a ventilator for 1 day and extubated after 48 h. The colostomy started functioning on day 5. The long-term plan is to work up for the nonvisualization of the left kidney. Distal cologram at 3 months of age and staged anal reconstruction.

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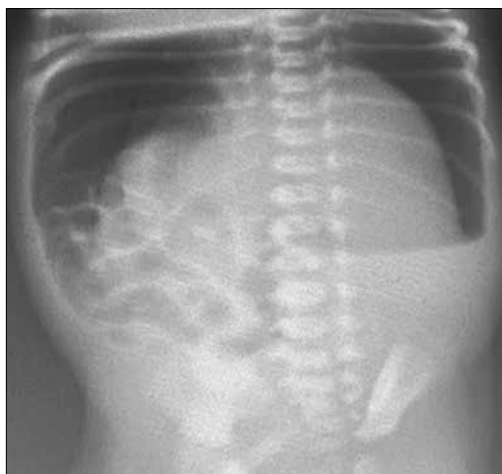


Figure 1: Pneumoperitoneum with football sign



Figure 2: Meconium in peritoneum



Figure 3: Perforation of the blind pouch of rectum sutured

DISCUSSION

Anorectal malformations occur in approximately 1/3000 live births and are more frequent in males.^[4] Local examination of the perineal region is often enough to confirm the diagnosis.

The primary intention in this baby is to follow the descent of gas shadow up to the rectum and decide the type of anorectal malformation (high/intermediate/low) followed by surgical intervention. The usual period for the gas shadow to descend till the rectum is approximately 18–24 h before we decide on the mode of surgical intervention.

Here, to our surprise, at 18 h of life, the baby had developed pneumoperitoneum (perforation of the blind pouch of the rectum). Prompt diagnosis and immediate exploratory laparotomy, closure of perforation, and sigmoid colostomy were done.

Delay in diagnosis of anorectal malformation is not uncommon. Spontaneous perforation of the colon is a rare complication, estimated to occur in 2% of neonates, but rises to 9.5% when diagnosis is delayed.^[2] Bowel perforation increases the neonatal mortality from 3% to 23%.^[1]

CONCLUSION

Very few cases have been reported about perforation in anorectal malformation and rectal perforations being the rarest among them. An early diagnosis with serial X-rays of the abdomen is important for anorectal malformation, mainly to give better results and prevent complications.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

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Conflicts of interest

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Case Report

Strategic management of posthysteroscopy pelvic abscess

ABSTRACT

This case report details the presentation, diagnosis, and management of a 32-year-old nulligravida who presented with lower abdominal pain, fever, and vomiting for 2 days. The patient had a history of pre-*in vitro* fertilization hysteroscopy 1 week back and laparoscopic ovarian cystectomy and ovum pickup in the past 5 months. Initial examination revealed severe tenderness in the left iliac region and an ill-defined mass in the left adnexa. Ultrasound and magnetic resonance imaging confirmed left ovarian endometriotic cysts with bilateral kissing ovaries. Conservative management with antibiotics and symptomatic treatment stabilized the patient, but subsequent laparoscopy revealed extensive bowel and omental adhesions, resulting in a frozen pelvis. Adhesiolysis and drainage of a pus-filled abscess were performed. Postoperatively, the patient recovered well and was discharged on the third postoperative day. Follow-up transvaginal ultrasound after 1 month showed no evidence of pelvic collection. This case underscores the importance of considering potential complications following hysteroscopy, especially in patients with a history of pelvic surgeries, and highlights the successful management of a complex clinical scenario involving pelvic abscess and frozen pelvis.

Keywords: Adhesiolysis, laparoscopic ovarian cystectomy, tubo-ovarian abscess

INTRODUCTION

Postoperative infection after hysteroscopy is uncommon. However, patients who have a history of pelvic inflammatory disease (PID) appear to be at risk of developing such infections, including tubo-ovarian abscesses (TOA). TOA is an inflammatory mass involving the fallopian tube, ovary, and occasionally other adjacent pelvic organs (e.g., bowel and bladder). TOA most commonly occurs in women of reproductive age. Upper genital tract infections and acute or chronic PID are the primary causes in most cases. Classically, a TOA manifests with an adnexal mass, fever, elevated white blood cell count, lower abdominal-pelvic pain, and/or vaginal discharge. However, presentations of this disease can be highly variable. If abscess ruptures, life-threatening sepsis can result. TOA may require more prolonged intravenous antibiotics and hospitalization. Typically, management consists of antimicrobial therapy with surgery reserved for cases with a poor response to antibiotics or for cases with suspected TOA rupture.

CASE REPORT

We present a case of a 32-year-old nulligravida who came with a complaint of posthysteroscopy lower abdominal pain associated with fever and vomiting for 2 days, bowel and bladder habits are regular. Menstrual cycles are regular and normal. She is planning for *in vitro* fertilization (IVF), so underwent pre-IVF hysteroscopy at a hospital 1 week back and had a history of laparoscopic ovarian cystectomy 5 months back and ovum pickup 2 months back. She had high-grade fever with other vital signs within normal limits, and an abdominal examination revealed severe tenderness

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in the left iliac region. Speculum examination revealed cervix and vagina healthy. On pelvic examination, the uterus was anteverted, bulky, tender, and nonmobile, and an ill-defined, tender, and firm mass of around 7 cm × 5 cm was palpated in the left adnexa with limited mobility. There was severe tenderness in all forniceal regions.

Ultrasound revealed left ovarian endometriotic cysts of size 75 mm × 75 mm and 58 mm × 55 mm with bilateral kissing ovaries. Her total leukocyte count was 22,300/uL. Magnetic resonance imaging reports suggestive of a bulky uterus with endometriotic cysts in the left adnexa. The patient was started on conservative management with higher antibiotics, antipyretic, and symptomatic treatment. The patient got stabilized after 48 h and discharged with a course of antibiotics. After 1 week, she is taken up for laparoscopy and proceeds with a differential diagnosis of to mass or endometriotic cyst. Laparoscopy findings revealed extensive and dense bowel and omental adhesions to uterus and bilateral adnexa obliterating postoperative day (POD) resulting in a frozen pelvis [Figure 1]. Adhesiolysis was done and the bowel was separated from uterus and adnexa. During the process, huge pocket of pus drained from POD. There was another 7 cm × 6 cm thick-walled abscess mimicking ovarian cyst [Figures 2 and 3]. Left adnexa presents posterior to abscess with no clear demarcation [Figure 4]. Abscess drained out and thorough irrigation done [Figure 5]. The right ovary was normal, right tube unhealthy. Bowel integrity was checked and found intact. Drain kept. Postoperative period was uneventful; the patient got discharged on the 3rd POD in stable condition. Follow-up advised and transvaginal ultrasound was done after 1 month. There was no evidence of collection in the pelvis [Figure 6]. Treatment of PID primarily should be with antibiotic; however, if there is no response in 3 days or the clinical diagnosis remains unclear further management of laparoscopy has to be considered for both diagnostic and therapeutic purpose.

DISCUSSION

Infection following hysteroscopic surgery is uncommon and has been estimated to be occurred in 0.18%–1.50% of cases.^[1] A practice bulletin of the American College of Obstetricians and Gynecologists suggests that antibiotics are of no value in general patients undergoing hysteroscopic surgery.^[2] However, prophylactic antibiotics are commonly used for hysteroscopic surgery. The risk of posthysteroscopy infection increases in patients with known risk factors, such as nulliparity, active bacterial vaginosis, previous pelvic surgery, multiple sexual partners, or history of PID.^[3,4] TOA is most frequently induced by ascending infection through



Figure 1: Frozen pelvis with dense adhesions

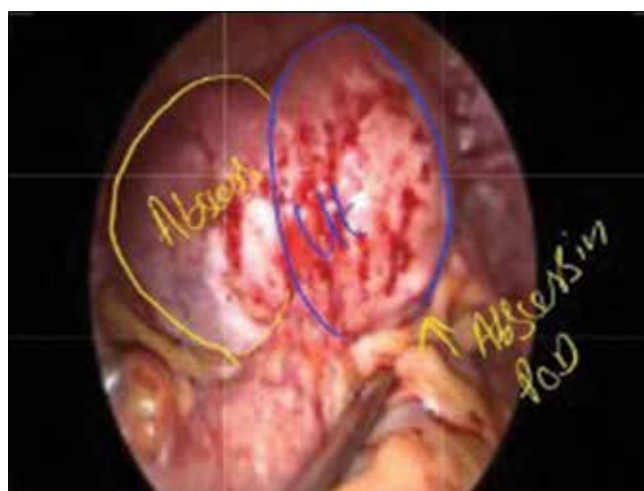


Figure 2: Pictorial depiction of uterus and adjacent abscesses



Figure 3: Draining of pus from pelvic abscess

the uterus due to *Neisseria gonorrhoeae*, chlamydia, *Escherichia coli*, or indigenous bacteria of the vagina and cervix, and it usually follows PID.^[5,6] Clinical signs of TOA such as lower abdominal tenderness, abnormal vaginal or cervical



Figure 4: Abscess in the left adnexa



Figure 5: Adhesiolysis



Figure 6: Postadhesiolysis final picture

discharge, fever, abnormal vaginal bleeding, dyspareunia, cervical motion tenderness, and adnexal tenderness^[7,8] and laboratory investigations such as the presence of excess

leukocytes and/or C-reactive protein.^[9] The management of TOA is a fundamentally conservative treatment with systemic broad-spectrum antibiotics. However, a TOA can have serious and potentially life-threatening consequences when there is a risk of abscess rupture. In such cases, antibiotic therapy is not sufficient for treating the TOA, and surgical drainage must be performed.^[7,10,11]

In the present case, even though the patient had diagnostic hysteroscopy, with a previous history of surgery and with ongoing infertility treatment (ovum pick up) Scan endometriotic cyst, high index of suspicion of PID with TOA suspected as she presented with typical signs and symptoms of to mass and with leukocytosis. In our experience, the diagnosis of pelvic abscess should be a clinical one. Imaging is prone to subjective variation and should be correlated clinically. Treatment of TOA is important to avoid complications such as life-threatening abscess rupture and sepsis and to preserve fertility, so early detection and treatment of TOA can prevent such adverse outcomes. Hence, in the present case, the patient was started on antibiotics and symptomatic treatment and taken up for laparoscopy and proceed after conservative management.

CONCLUSION

Timely intervention of laparoscopy offers the possibility to diagnose and manage PID safely and prevents complications and often preserves the patient's fertility. Early intervention also can pose problems such as unnecessary bowel injuries. One should rely on clinical findings as imaging technology may mislead the diagnosis sometimes.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

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Case Report

Wernicke's aphasia as the primary presenting feature in a young stroke female with antiphospholipid syndrome – The first ever case report from India

ABSTRACT

Wernicke's aphasia is a language disorder characterized by fluent speech with impaired comprehension and is traditionally associated with damage to the left posterior superior temporal gyrus. This article aims to explore the unique aspects of Wernicke's aphasia in the context of stroke in young patients. To the best of our knowledge, this is the first case report of Wernicke's aphasia as the primary and solo presentation in a young stroke patient with antiphospholipid syndrome.

Keywords: Antiphospholipid syndrome, autoimmune disease, stroke, Wernicke's aphasia, young female

INTRODUCTION

Wernicke's aphasia, also known as receptive aphasia, is referred to a condition, in which there is trouble in understanding spoken and written language. In roughly 95% of right-handed people and 70% of left-handed people, the most frequent cause of occurrence is damage to the posterior superior temporal gyrus, a part of the dominant cerebral hemisphere (Brodmann's area 22).^[1] Unlike Broca's aphasia, in Wernicke's aphasia, patients may exhibit fluent speech, along with proper grammar and normal sentence structure. However, they may also use extended, meaningless sentences, extra words, or even make up their own words. Neurological symptoms depend on the size and location of the lesion that include visual field deficits, trouble with calculation (acalculia), and writing (agraphia). In most patients, the root cause of this kind of aphasia is an embolic or ischemic stroke affecting the inferior division of the middle cerebral artery (MCA), supplying the temporal cortex.

CASE REPORT

A 29-year-old female visited our hospital with a chief complaint of sudden onset of difficulty in speaking and comprehending

words, repetition of irrelevant words and sentences, difficulty in understanding and following orders or commands, and also reading and writing and restlessness for the last 6 h. There was no history of headache, loss of consciousness, nausea or vomiting, limb weakness or deviation angle of the mouth, vision disturbance, or transient ischemic attack (TIA). There was no history of fever, night sweats, loss of appetite, or weight loss. She had no history of hallucinations or abnormal behavior before and no record of any psychiatric illness.

On examination, there was no pallor, cyanosis, clubbing, pedal edema, lymphadenopathy, or thyroid swelling. Vitals were within the normal limits (pulse rate – 78/min and blood pressure – 124/80 mmHg). Central nervous system

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examination – the patient was conscious but irritable and agitated. Her speech was evaluated as spontaneous speech with good fluency (repetitive talks and neologism present) repetition – impaired, comprehension – impaired, naming – impaired, and reading and writing – not cooperative.

Pupils bilateral – 3 mm reactive, fundus – normal, extraocular muscle – full, no ptosis, no facial lag, other cranial nerves examination – normal, motor system: tone – normal, power 5/5 all 4 limbs, deep tendon reflexes – 2+, plantar – flexors, sensory – could not be assessed, no cerebellar signs, no meningeal signs/no neck stiffness, other systemic examination – normal.

There was no significant medical history except the history of spontaneous abortion (first trimester) 2 years back. Routine blood investigations and two-dimensional echo were normal. Vitamin B12 level was significantly low at 80 pg/ml corresponding to her purely vegetarian diet. Magnetic resonance imaging (MRI) brain was suggestive of acute infarct in the left temporoparietal region involving the inferior branches of the M2 segment of left MCA [Figure 1a and b]. However, MRI angiography and venogram were normal.

Considering the young age of the patient and history of spontaneous abortion, antinuclear antibody (ANA) blot and thrombophilia profile with antiphospholipid antibodies (APLAs) antibody were sent. Homocysteine levels were found to be >50. As she presented after 6 h of the onset of symptoms (beyond the window period), thrombolysis was not considered in management. Meanwhile, she was treated conservatively with anti-coagulants and anti-platelets and was given the support of speech therapy. The patient showed improvement and started recognizing, understanding, and partially obeyed commands. Reading and writing were significantly improved within 3 days of starting treatment. Workup for the previously sent autoimmune disorder revealed a high titer of anti-β2 glycoprotein 1 (β2GPI) IgG (79 U/mL) shown in Figure 2a and anti-cardiolipin IgG was negative (1.5 U/mL) antibodies, and a low titer of anti-β2GPI (2.3 U/mL); whereas antiplatelet antibodies, ANA, anti-double stranded-DNA, anti-mitochondrial antibodies, antineutrophil cytoplasmic antibodies, anti-liver-kidney microsomal antibodies, and anti-smooth muscle antibodies were negative. lupus anticoagulant (LAC) was also found to be positive [Figure 2b]. The ultrasound abdomen examination was normal. A cardiology workup was performed by an experienced cardiologist of our institute and was found to be within normal limits. The anticoagulation therapy was carried on with good response and then shifted to oral anticoagulation therapy. Anti-β2GPI IgG and LAC were repeated after 12 weeks and were found to be positive, hence confirming our diagnosis [Figure 3].

DISCUSSION

This case underscores the complexity of young-onset ischemic stroke. Ischemic stroke and TIAs are the most common neurologic complications in patients with APLA. Although the neurologic presentation of patients with antiphospholipid syndrome (APS) may vary, many patients have striking similarities, such as initial memory loss, aphasia, cognitive dysfunction with progressive cerebral deterioration, and even dementia. The identification of anti-β2GPI, IgG, and LAC helps in identifying the APS. APS is an autoimmune disorder recognized in its association with recurrent thrombotic events and pregnancy-related complications.^[2] Elevated homocysteine levels are the risk factors for the hypercoagulability. The response to the anticoagulation

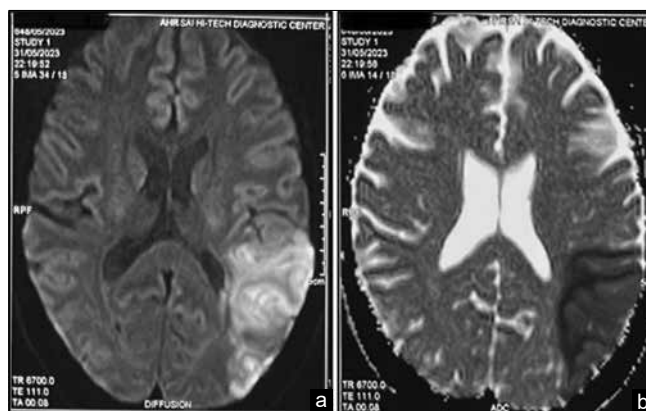


Figure 1: (a) Magnetic resonance imaging showing diffusion restriction in inferior division of M2 of left middle cerebral artery, (b) Apparent diffusion coefficient sequence confirms acute infarct in same area

Investigation	Observed Value	Unit	Biological Reference Interval
DRVV Screen Ratio	1.72	--	0.85-1.20
DRVV CONFIRM (Citrated plasma)			
DRVV Confirm (Test) (Method-Clot Based)	41.2	sec	31.04-40.55
DRVV Confirm Control	35.0	sec	--
DRVV Confirm Ratio	1.18	--	0.89-1.16
Normalized Ratio	1.48	--	<= 1.20
LUPUS ANTICOAGULANT (Citrated plasma)			
LUPUS ANTICOAGULANT	PRESENT		Absent
Medical Remarks: See Remark - 4. Correlate clinically.			
Investigation	Observed Value	Unit	Biological Reference Interval
Thrombophilia Profile-Maxi**			
Thrombophilia Profile-Maxi			
Beta-2-Glycoprotein 1-IgG (Serum, Fluorescent immunoassay)	Positive, 79	U/mL	Negative: < 7.0 Positive: > 10.0 Weak Positive: 7.0-10.0 Please note change in Reference range, method and unit

Figure 2: (a) Lupus Anti-Coagulant Positive. (b) Beta 2 Glycoprotein 1 IgG Positive

Test Name	Test Report Results	Units	Bio. Ref. Interval
PHOSPHOLIPID SYNDROME PANEL WITH BETA 2 GLYCOPROTEIN 1, 1HR			
BETA 2 GLYCOPROTEIN 1, IgG SERUM (EIA)	54.36	SGU	<20.00

Figure 3: Follow-up investigations

1 therapy with the established management approach to
2 APS helps to prevent recurrent thrombotic events.^[3,4] Low
3 Vitamin B12 levels might have been one of the causes for
4 her neurological symptoms.^[5]

5
6 According to several studies, in young (<45 years of age),
7 only a handful of 20% of strokes are potentially associated
8 with APS. A multitude of neurological problems such as
9 convulsions/epilepsy, dementia, cognitive deficits, headaches/
10 migraine, chorea, multiple sclerosis-like symptoms, transverse
11 myelitis, ocular symptoms, Guillain–Barré syndrome, and
12 even peripheral neuropathy can be presenting features of
13 APS. Wernicke's aphasia is almost never the first presenting
14 symptom in such cases. However, our timely diagnosis and
15 prompt intervention allowing a multidisciplinary approach to
16 incorporating anticoagulation therapy and speech therapy to
17 the patient helped in significant improvement in a short time.
18 In such cases, regular follow-ups are essential to adjust the
19 management plan and to monitor the patient's response to the
20 treatment. The long-term use of anticoagulation therapy aims
21 at preventing recurrent thrombotic events in these patients.^[6,7]

22 23 CONCLUSION

24
25 On the basis of medical history, clinical and laboratory
26 features, and ruling out associated autoimmune diseases,
27 a diagnosis of primary APS was made. To the best of our
28 knowledge, this is the first case report of Wernicke's aphasia
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as the primary and solo presentation in a young stroke patient
with APS in the Indian population.

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Conflicts of interest

There are no conflicts of interest.

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Case Report

Coiling and liquid embolization of a carotid-cavernous fistula

ABSTRACT

A carotid-cavernous fistula (CCF) results from an abnormal vascular shunt between the carotid artery and the venous channels of the cavernous sinus. The clinical presentation varies based on the involved neurovascular structures, the anatomy of the shunt, the underlying cause, and the hemodynamics of the CCF. In this case report, we describe a 46-year-old man who presented with recurrent headaches, redness, bulging, and a rapid decline in vision in his right eye, along with diplopia. Brain magnetic resonance imaging revealed dilation of the superior ophthalmic vein. A subsequent digital subtraction angiogram confirmed a Barrow classification Type D (indirect) CCF. The patient underwent endovascular therapy involving combined coil and Onyx™ embolization (a mixture of ethylene-vinyl alcohol copolymer, dimethyl-sulfoxide, and micronized tantalum powder from Medtronic, USA) intervention resulting in an exceptional angiographic and clinical outcome. The patient became entirely symptom-free within 2 weeks following the treatment.

Keywords: Carotid-cavernous fistula, cavernous sinus, coil embolization, digital subtraction angiogram, endovascular therapy, Onyx embolization, transvenous approach

INTRODUCTION

A carotid-cavernous fistula (CCF) arises due to an abnormal vascular connection between the carotid artery and the venous channels within the cavernous sinus (CS).^[1] The clinical manifestations vary depending on the specific involvement of neurovascular structures within the sinus.^[2] Left untreated, these fistulas can lead to potentially devastating consequences such as vision loss, subarachnoid hemorrhage, intracerebral hematoma, and progressive proptosis.^[3] Spontaneous occurrences of CCFs are rare, and their precise incidence remains unknown.^[2] Within our report, we highlight a case involving a spontaneous Type D (indirect) CCF. This case was successfully managed through transvenous endovascular therapy (ET).

CASE REPORT

The patient is a 46-year-old male, a known diabetic on regular treatment with good compliance, maintaining a nonsmoking, nondrinking lifestyle. He had no history of prior head or faciomaxillary trauma. Three weeks before

seeking medical attention, the patient started experiencing headaches and observed redness in his right eye. Initially, he received eye drops (antibiotics, steroids, and artificial tears) and analgesics from his local practitioner. However, even after 2 weeks of this treatment, there was no noticeable improvement in his symptoms. However, a sudden onset of bulging accompanied by rapidly declining vision in

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the right eye and double vision occurred 1 week before the presentation [Figure 1]. The patient promptly sought care from a nearby ophthalmologist, who conducted a comprehensive ocular examination. Examination of the left eye showed slight chemosis, conjunctival injection, a 3 mm pupil with intact light reflexes, and a visual acuity of 6/24. On examination of the right eye, pronounced conjunctival injection and chemosis, a 3.5 mm pupil with intact direct and indirect light reflexes, and nonaxial proptosis with restricted ocular movements – particularly abduction – were noted. The visual acuity in the right eye was measured at 6/60. Tono-Pen tonometry indicated increased intraocular pressure in the right eye. Fundoscopy revealed papilledema and retinal venous engorgement in the right eye. Considering the clinical presentation and ocular findings, a preliminary diagnosis of a CCF was suspected. Subsequent brain magnetic resonance imaging (MRI) depicted significant enlargement of the right superior ophthalmic vein (SOV) [Figure 2]. Consequently, the patient was transferred to the neurovascular intervention department for further management. A digital subtraction angiogram (DSA) was performed, revealing a Type D CCF with an early filling of the right CS in the arterial phase [Figure 3]. Given the rapidly deteriorating clinical condition, shunt anatomy, and hemodynamics, the decision was made to embolize the CCF.

Procedure

The patient was placed supine on the angiographic table. The patient was intubated, and the procedure was performed under general anesthesia following a strict aseptic protocol. A simultaneous right transfemoral venous and left transfemoral arterial access was taken. A 5F diagnostic catheter from the left groin puncture was placed at the common carotid artery. A 5F diagnostic catheter was navigated from the right transvenous groin access through the inferior vena cava, right atrium, superior vena cava, and jugular vein. At the level of the jugular sigmoid junction, a microcatheter was maneuvered into the inferior petrosal sinus (IPS), leading to the CS. After cannulating the CS, an angiogram was performed to confirm the position of the microcatheter. Embolization was done with Onyx on the left side and coils on the right side of the CS [Figure 4]. The final angiogram demonstrated occlusion of the CCF with arterial branches within the normal limits [Figure 5]. The procedure was completed and the patient was extubated without any new neurological deficit. A total of five coils and 2 ml of Onyx were used to achieve complete embolization.

There was a significant improvement in the vision, diplopia, and redness in both eyes within 48 h postprocedure [Figure 6]. The patient was discharged on the 3rd day postoperatively. At his 2nd week follow-up, the patient's ocular redness,



Figure 1: Clinical image showing chemosis, conjunctival injection, and slight proptosis of the right eye

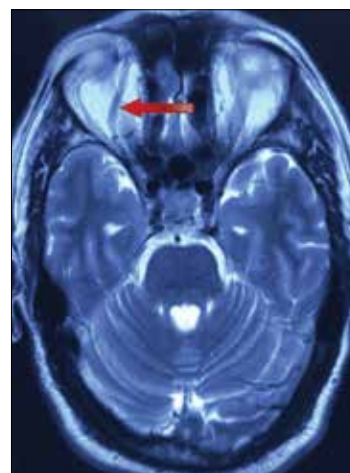


Figure 2: Brain magnetic resonance imaging, axial view, demonstrating a dilated superior ophthalmic vein (red arrow)



Figure 3: Digital subtraction angiogram revealing a carotid-cavernous fistula with an early filling of the right cavernous sinus in the arterial phase

proptosis, headaches, and visual disturbances have completely resolved.

DISCUSSION

CCFs can be categorized according to several factors: shunt anatomy (direct vs. indirect), etiology (traumatic vs. spontaneous), and hemodynamics (high flow vs. low flow).^[2] Barrow *et al.* established a classification system for CCFs

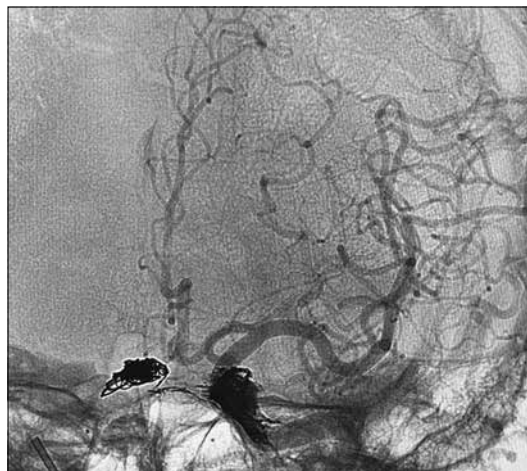


Figure 4: Digital subtraction angiogram cerebral angiogram showing the placement of coils on the right side and Onyx embolization on the left side

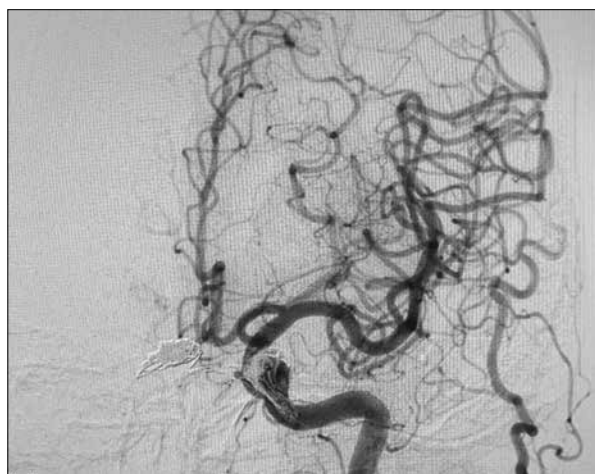


Figure 5: The final check angiogram demonstrating occlusion of the carotid-cavernous fistula with normal arterial flow



Figure 6: Clinical picture 48 h postoperatively showing a noticeable reduction of the right eye redness within 48 h postprocedure

based on the involved arterial system [Table 1]. Type A CCFs represent direct fistulas, while types B, C, and D are categorized as indirect.^[4] Indirect CCFs are considered low-flow variants because they originate from dural branches rather than the high-flow internal carotid artery (ICA).^[2] In 2015, Thomas *et al.* proposed an updated classification system based on venous drainage [Table 2].^[5]

CCFs occur when high-pressure blood from the arterial system (ICA or external carotid artery) is shunted into a low-pressure venous system, specifically the CS, without an intervening capillary bed to reduce the pressure. This pressure disparity and vascular resistance obstruct venous drainage, causing congestion in the areas drained by the CS.^[6] Ophthalmic manifestations, commonly observed, may take several days to weeks to develop as venous hypertension needs to reach critical levels before becoming apparent.^[7]

The classical clinical triad consists of chemosis, proptosis (pulsatile exophthalmos), and ocular bruit.^[8] They are less frequent in indirect CCFs. Other observable features include headache, pain (ocular/periorbital), proptosis, cephalic bruit, pulsatile tinnitus, loss of visual acuity, raised intraocular pressure, secondary glaucoma, ophthalmoplegia, trigeminal nerve dysfunction, anhydrosis, otorrhagia, and epistaxis.^[7,9,10] In our patient, his initial atypical and seemingly mild presentation might have led to the erroneous diagnosis and treatment earlier on. Conjunctivitis, nonspecific orbital inflammation, orbital/retrobulbar hemorrhage, orbital infection, Grave’s ophthalmopathy, orbital tumor, tumor with CS involvement, orbital vasculitis, orbital apex syndrome, CS thrombosis, and

Table 1: Barrow classification

Type	Description
A	Direct connection between the ICA and CS
B	Connection between meningeal branches of ICA and CS
C	Connection between meningeal branches of ECA and CS
D	Connection between meningeal branches of both ICA and ECA and the CS

CS: Cavernous sinus, ECA: External carotid artery, ICA: Internal carotid artery

Table 2: Thomas classification of carotid-cavernous fistula by venous drainage

Type	Description
1	Posterior/inferior venous drainage only
2	Posterior/inferior and anterior venous drainage
3	Anterior venous drainage only
4	Retrograde cortical venous drainage
5	Direct ICA-CS fistulae corresponding to the type of barrow classification

CS: Cavernous sinus, ICA: Internal carotid artery

superior orbital fissure syndrome are some of the probable differential diagnoses for a case of CCF.^[9]

Ocular Doppler ultrasound can be a helpful screening tool. It can identify the dilation and flow velocities within the SOV, as well as the enlargement of the extraocular muscles.^[11] A plain computed tomography (CT) is more helpful in CCF cases with a history of trauma as it is more sensitive in detecting basilar skull fractures. CT with contrast can reveal SOV dilation and proptosis. An MRI is superior to CT in delineating abnormal flow voids or orbital edema.^[12] CT angiogram and magnetic resonance angiogram (MRA) are the first-line noninvasive imaging modalities in evaluating CCFs, particularly those with visual symptoms.^[1,13] However, in our case, an MRA was not performed and we directly opted for a DSA. Although invasive, DSA is the gold standard imaging modality. It can identify the location, arterial supply, venous drainage, and flow rate to classify the CCF and help plan for potential ET strategies.^[11,14]

Endovascular intervention is widely considered the first-line treatment of CCFs. Recent technological advances have increased the number of safe and viable treatment options, with a cure rate of well over 80%.^[2] Surgical intervention is the most invasive option available. Success rates range from 31% to 79% and depend on the method, approach, and skill of the operator.^[1] Surgery is associated with higher perioperative risks, residual fistulous communications, and complications like cranial nerve palsies. Nowadays, it is primarily indicated as salvage for failed ET.^[7] Awaiting spontaneous closure, compression treatment or stereotactic radiosurgery are other viable alternatives for select cases with low-flow indirect fistulas.^[1,2,7,15] However, these treatments are associated with a considerable time lag for the resolution of symptoms, which excludes them as an option for emergencies with rapid deterioration, as with our patients.

Transvenous procedures are the preferred treatment approach for indirect fistulas because of their simplicity, higher success rates, lower ischemic risk, and capability to cure the fistula in a single session. In the transvenous approach, the abnormal CS is super selectively catheterized and the fistula is occluded without rerouting venous drainage to the cortical structures.^[16] IPS is the most commonly used venous pathway for cannulation of the CS. Less commonly, in some technically inaccessible cases, the anterior approach through the SOV through the facial vein lateral pterygoid plexus, superior petrosal sinus, cortical veins, the inferior ophthalmic vein, or the contralateral IPS or SOV with access into the ipsilateral CS through the circular sinus.^[7,16]

After successful cannulation of the CS, embolization can be achieved with materials such as coils, n-butyl 2-cyanoacrylate, and ethylene-vinyl alcohol copolymer (EVOH), either alone or in combination. We used a combination of coils and EVOH. Coils are radiopaque, easy to use, and can be redeployed or removed if the initial placement is not optimal. However, adequate volumetric packing or complete occlusion is not always achievable. Concomitant use of EVOH has the ability of mechanical occlusion without vessel wall adhesion. Its nonadhesive nature decreases the risk of microcatheter retention and allows a slow single injection of the embolic agent with concomitant angiogram checks.^[16,17]

Successful closure of the CCF results in rapid elimination of the vascular pressure head and alleviates the ocular manifestations produced by the venous congestion.

CONCLUSION

CCF is a rare vascular phenomenon which is capable of atypical presentations, compounding the complexity of its management. A high index of suspicion is necessary for prompt diagnosis and appropriate therapy, which is vital for achieving the best possible visual and neurological outcomes.

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Conflicts of interest

There are no conflicts of interest.

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Case Report

Evaluation and management of obstructive suprastomal granulation tissue

ABSTRACT

Suprastomal granulation tissue can result in bleeding and difficulty in replacing tracheostomy tube. It delays decannulation and may interfere with ventilation. Granulation tissue formation is generally a consequence of rather than a complication of tracheostomy. Evaluation and management of two cases of obstructing suprastomal granulation tissue are presented. A 7-year-old child and a 58-year-old female who presented with an obstructing suprastomal granulation tissue due to prolonged use of tracheostomy, they were managed with radiofrequency ablation-assisted excision and serial balloon dilatation. Both patients were followed over a period of 3 months, with regular flexible endoscopy. After ensuring the healing and patency of the airway tract, they were decannulated as per protocol. These two cases emphasize early detection of the suprastomal granulation tissue in patients with prolonged use of tracheostomy and regular follow-up with flexible endoscopy to ensure optimal long-term outcome after surgery.

Keywords: Balloon dilatation, case report, flexible endoscopy, granulation tissue, radiofrequency ablation, suprastomal

INTRODUCTION

The origin of the suprastomal lesions may be related to cartilage trauma during the procedure, friction from the tube itself, infection, or pooling of secretions in this area.^[1] Although small, nonobstructing granulomas do not require removal given their high recurrence rate and the low morbidity associated with them. Larger granulomas are associated with a much higher morbidity, from bleeding, poor voice production to accidental decannulation. Many techniques have been described for granuloma removal, including endoscopic with the help of laser, radiofrequency (RF) ablation, forceps, and open excision. There are challenges to all of these techniques, and one has not proven to be superior to the rest. The use of any laser brings an attendant risk of airway fire. Forceps and other techniques may be associated with increased bleeding as well as the possibility of tissue loss into the lower airways.

CASE REPORTS

Case 1

A 7-year-old child who came for plastic surgery could not be intubated due to Grade 1 glottic web. Tracheostomy

ventilation was used for multiple plastic procedures. Glottic web was released by an ENT team. Two months later, extubation failed multiple times. The child was then referred for decannulation. Virtual bronchoscopy and computed tomography (CT) of the neck revealed a Grade 3 glottic stenosis [Figure 1a] and a suprastomal granulation tissue, releasing the stenosis without injuring the vocal cords was a challenge. Release of glottic stenosis, suprastomal granulation tissue excision with RF ablation, and serial balloon dilatation were performed [Figure 1b and c]. Mitomycin C was applied over the vocal cords to prevent adhesions. After 10 days, second-stage removal of the residual tissue with serial balloon dilatation was done. Regular flexible endoscopy was done in each visit, to

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look for healing and patency of the airway, he was safely decannulated and normal voice was restored.

Case 2

AQ8 A 58-year-old female with uncontrolled diabetes was on prolonged tracheostomy for surgical treatment of carcinoma of the buccal mucosa. On flexible endoscopic examination, large obstructing suprastomal granulation tissue was noted [Figure 2]. CT neck was done which showed diffuse circumferential soft-tissue thickening of the proximal trachea, involving a 2.2 cm length of the trachea and causing moderate luminal narrowing. RF ablation-assisted airway surgery was performed. She was placed in a supine position with number 6 size nonfenestrated tracheostomy tube *in situ*.

AQ9 Laryngoscope was fixed in position, with the help of RF ablation tissue was excised followed by balloon dilatation of the airway. The steroid was injected locally. The tracheostomy tube was downsized and eventually and safely decannulated in the subsequent visit. Postoperative flexible endoscopy revealed a patent airway.

DISCUSSION

Granulation tissue can result in hemorrhage (especially for patients receiving anticoagulants because of other medical problems), difficulty in replacing the tracheostomy tube in instances of accidental dislodgement of the tracheostomy tube, and delay in decannulation and may result in obstruction of the tracheostomy tube. Several deaths have also been reported.^[2] It can form around the stoma, suprastomal area, within the trachea, and in the trachea at the tip of the tracheostomy tube. Movement of the tube within the stoma and tracheal lumen may cause ulceration and increase the likelihood of bacterial colonization and development of granulation tissue.^[4]

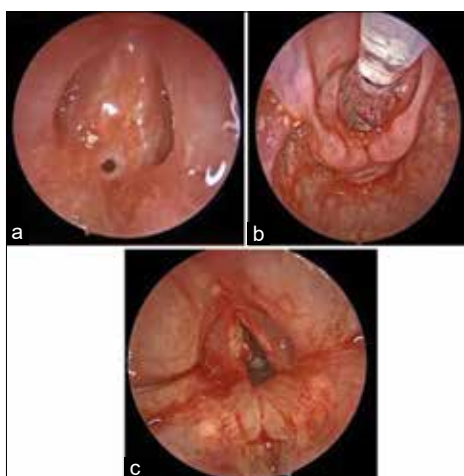


Figure 1: (a) Glottic stenosis, (b) After adequate dissection laryngeal balloon dilator used, (c) Postsurgery – Near-normal laryngeal opening

Granulation tissue occurs during a proliferative stage of inflammation resulting in polypoid vascularized tissue. Often, the lesion can be pedunculated and may obstruct the tracheostomy, causing problems with ventilation and replacement of the tube. On histological section, vascularized and inflamed granulation tissue with loose edematous stroma is seen. The surface is ulcerated and covered by fibrin debris. Bacterial infection, gastroesophageal reflux, the presence of powder from surgical gloves, and the use of stents in laryngotracheal reconstruction have been implicated as causes of granulation tissue formation. Until recently, *Staphylococcus epidermidis* was considered a contaminant rather than an infectious agent. The pathogenesis of a foreign body-associated infection with *S. epidermidis* is colonization of the surface by formation of a biofilm.^[5]

When granulation tissue becomes obstructive, preventing ventilatory support, surgical intervention should be considered.^[6] The use of bronchoscopy equipment in conjunction with excision has been described as a safe, reliable method for removal of suprastomal granulation tissue. No studies have been performed to assess the efficacy of each treatment in a specific patient population. The tracheostomy tube can be viewed as an indwelling catheter and, like all foreign bodies, elicits an inflammatory response from the tissue. The presence of a foreign body in the trachea stimulates mucus production and affects the mucociliary stream. Mucosal metaplasia occurs over the long term with loss of ciliated cells. This change in normal physiology predisposes to the development of granulation tissue.

CONCLUSION

Early detection of granulation tissue at the tracheostomy site can prevent serious airway complications. In patients with prolonged use of tracheostomy, good hygiene around the



Figure 2: Suprastomal granulation tissue measuring 1.99 cm x 0.98 cm

1 stoma and frequent tube change must be ensured. In case of
 2 pus from the stoma site, it should be evaluated and treated
 3 immediately. **Once the patient is planned for decannulation,**
 4 **before that an airway assessment can be done to confirm the**
 5 **patency of the airway.** Moreover, if the patient underwent
 6 airway surgery, periodic follow-up over 3 months is required
 7 to ensure that the tract is patent and healed.

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 12 **Conflicts of interest**

13 There are no conflicts of interest.
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