ORIGINAL ARTICLE

ADVANCES IN DIAGNOSIS, TREATMENT AND PROGNOSTIC IN AORTOILIAC OCCLUSIVE DISEASE – A NARRATIVE REVIEW

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Abstract

Background: *Aortoiliac disease (AID) is a variant of peripheral artery disease involving the infrarenal aorta and iliac arteries. Similar to other arterial diseases, aortoiliac disease obstructs blood flow through narrowed lumens or by embolization of plaques. AID, when symptomatic, may present with a triad of claudication, impotence, and absence of femoral pulses, a triad also referred as Leriche Syndrome (LS).*

Objective: *The authors aim to review the available evidence on the management of the aortoiliac occlusive disease and describe its clinical characteristics, diagnosis and treatment management.*

Methods: *A comprehensive review of the literature was carried out to collect data from relevant studies concerning patients with moderate to severe symptomatic aortic occlusive disease. The data was identified by a search using PubMed and Google Scholar with the keywords / MESH terms "aortoiliac occlusive disease". For this study, the authors included papers published in the past two decades, written in English.*

Results: *The diagnosis and evaluation of extensive aortoiliac disease involves several important considerations: vascular imaging plays a fundamental role in confirming the diagnosis of peripheral artery disease (PAD), evaluating the severity and extent of the disease and directing the planning of revascularization procedures. It provides essential information to select the most appropriate treatment modality.*

Conclusion: *Despite successful revascularization, patients are at high risk of mortality and numerous life-threatening complications. Clinical and imagiologic factors may be used for risk stratification in order to select appropriate patients for revascularization and to better counsel patients about expected postoperative outcomes.*

Keywords: *Aortoiliac stenting; perioperative care; Arterial Occlusive Diseases* / diagnostic imaging; Arterial Occlusive Diseases* / surgery; Iliac Artery / diagnostic imaging; Iliac Artery / surgery; Stents*

INTRODUCTION

Aortoiliac disease (AID) is a variant of peripheral artery disease (PAD) affecting the infrarenal aorta and iliac arteries.

Severe aortoiliac stenosis or occlusion is often a chronic disease resulting from progressive atherosclerotic and thrombotic accumulation. While acute occlusions of the native aortoiliac system can occur, they are uncommon and a very different disease process associated with high morbidity and mortality [1, 2]. The management of these often critically ill patients is separate from the chronic setting. Chronic occlusions, however, progressively impair direct inflow to the pelvis and lower extremities. The chronicity of this process leads to the development of extensive collateral networks involving systemic pathways via the lumbar, intercostal, epigastric and circumflex iliac vessels, as well as visceral–systemic pathways through branches of the celiac, superior and inferior mesenteric arteries [3]. These collaterals allow many patients to present with significantly less severe symptoms than expected from such an advanced disease process.

Clinical indications for intervention include life-limiting claudication, rest pain and tissue loss. Less commonly, patients may be treated following atheroembolism from the aortic or iliac lesions, most often presenting with acute limb

ischemia or 'blue toe syndrome'. Approximately 45–65% of patients with AID present with claudication of the buttocks, thighs and calves[4, 5, 6, 7, 8]. The classic triad of claudication of the buttock and thighs, absent femoral pulses and impotence described by Leriche, also referred as Leriche Syndrome (LS), is noted in as many as 73% of men with AID[9]. More severe symptoms of critical limb ischemia with rest pain or tissue loss are less common due to collateralization; however, when present, they often suggest extensive iliac and infrainguinal vessel involvement. Acute worsening or onset of symptoms can develop following thrombosis of chronically diseased vessels or an embolic event.

Patient-reported outcome measurements (PROMs) are also essential tools in evaluating outcomes of different treatment methods in patients with QoL affection like in PAD. Additionally, these tools provide essential information to the health providers and the taxpayers for assessing health services [13].

Therefore, the aim of this work is to review the available evidence regarding diagnostic strategies, prognostic tools and management in the setting AID.

METHODS

The methodology of this comprehensive review followed adapted PRISMA guidelines to ensure transparency and rigor in the search and data collection process. The review aimed to identify studies related to patients with moderate to severe symptomatic aortic occlusive disease, focusing on new or non-established tools for diagnosis or treatment.

The data was identified through systematic searches conducted on PubMed and Google Scholar. Keywords and MeSH terms utilized in the search strategy included "aortoiliac occlusive disease." The search was limited to articles published in the past two decades and written in English. Inclusion criteria prioritized studies that addressed transversal diagnostic or therapeutic approaches used in other areas of knowledge, with particular attention to tools that are not yet fully established in clinical practice.

The search strategy was supplemented by manual screening of references from the retrieved articles to ensure comprehensiveness. Abstracts were screened to identify potentially relevant studies. Full-text articles meeting the inclusion criteria were then reviewed to extract pertinent data.

This approach facilitated the identification of relevant studies and ensured that the review's findings are based on a systematic and thorough examination of the available literature.

RESULTS

Diagnosis and prognostic tools of extensive aortoiliac disease

Vascular imaging confirms the diagnosis of PAD, assesses the severity and extent of disease, and is also used to plan and guide revascularization. Identifying high risk patients is an important step in the decision process of whether a patient would benefit from an intervention or even if there is any sarcopenic reversibility and preoperative optimization that can be provided. However, the ongoing research and subsequent clinical utility is being challenged by different definitions and the still undisclosed optimal frailty tool to use in vascular surgery and its subpopulations.

In vascular surgery settings, frailty and sarcopenia have been accepted as useful prognostic tools to evaluate patients' characteristics before surgery, as these may predict perioperative clinical and surgical outcomes[16]. In a prospective single center series of aortoiliac TASC D revascularization, envolving 57 patients with a mean age 60±8.2 years; range, the Psoas Muscle Area (PMA) was used as a threshold value. Cox proportional hazards modeling was used to estimate covariate association with all-cause mortality and indicated that the overall psoas area proved to be a prognostic indicator for both survival and significant adverse cardiovascular events[14]. Additionally, it facilitated a swift and precise evaluation with consistent results.

One possible definition for frailty is a physiologic decline associated with aging, vulnerability to adverse events and poor prognosis [16]. Frailty has been associated with short- and long-term mortality after major vascular surgery in elderly patients. Furthermore, it can also lead to an increase in health care costs for surgical patients [16].

Although minimally invasive surgical approaches, such as endovascular therapy and hybrid procedures have been universally developed, achieving good surgical outcomes for high-risk cohorts remains a challenge due to the increasing prevalence of elderly patients with multiple comorbidities in addition to frailty and sarcopenia.

Haematological parameters, such as the red blood cell distribution width (RDW), have recently been emerging as a tool to help predict patient outcomes[15]. RDW-CV is a widely available, easy to measure, and low-cost marker that independently predicts long-term mortality, MACE, and MI after aortoiliac revascularization. Even though the mechanisms underlying these associations are not yet fully understood, this factor could prove useful in assessing which patients would likely benefit from aortoiliac revascularization in the long term. Future research on this parameter should focus on a possible molecular basis, and interactions with inflammatory pathways, in order to shed light on the pathophysiologic mechanisms [15].

Myocardial injury after non-cardiac surgery may have a prognostic role in the postoperative period. One study reported that the incidence of myocardial injury after non-cardiac surgery was 25.8% after revascularization of aortoiliac TASC D lesions and chronic heart failure was associated with the presence of myocardial injury after non-cardiac surgery. In addition, myocardial injury after aortoiliac revascularization was a strong predictor of further myocardial infarction, stroke, acute heart failure, major adverse cardiovascular events, major adverse limb events, and all-cause mortality at a one-year follow-up[28].

Among the 1 to 2% of patients who develop

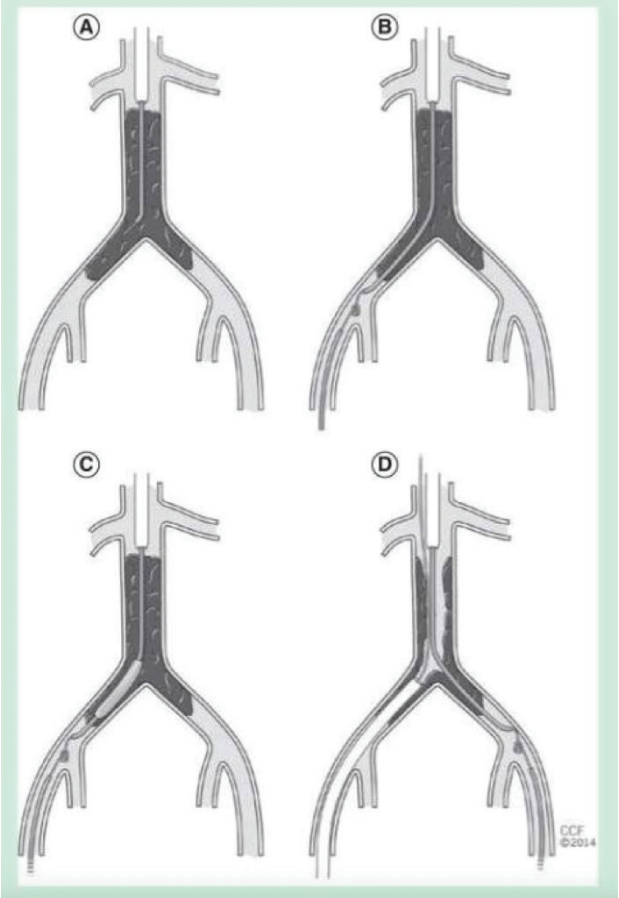

Figure 1

Representation of technique for crossing aortic occlusion and preparing fortreatment
(A) From the brachial approach, the sheath is advanced to the proximal edge of theocclusion and the wire is drilled through the occlusion with progressive advancement of the catheter. (B) After crossing the lesion, femoral access is obtained and the wire is snared to obtain through-and-through access. (C) A small angioplasty balloon is used to dilate the occlusion prior to sheath advancement. (D) The same technique is used on the contralateral side, followed by advancement of sheaths to the aortic bifurcation from the femoral arteries[1].

1 - Adpated from: Jm, G. CD, Beach. Strategies for managing aortoiliac occlusions: access, treatment and outcomes. Expert review of cardiovascular therapy. 2015;13(5).

chronic limb-threatening ischemia, outcomes have improved over time, related to improved medical management [46, 47], and possibly the more liberal use of endovascular intervention[48]. Even among those without a revascularization option, amputation-free survival has improved [(49)]. Overall, at one year, 45% of patients will be alive with both limbs, 30% will have undergone amputation, and 25% will have died. At five years, more than 60% of patients with CLTI will have died. For patients with nonreconstructible disease at one year, approximately 55% will be alive without amputation (range 40 to 69%); 20% of patients will have died (range: 12 to 32%), and 34% will have undergone major amputation (range: 25 to 45%)[18]. The prognosis for both limb loss and survival is significantly worse in patients with DM and end-stage kidney disease, and those who continue to smoke[50].

Management - Revascularization Procedures

Among patients with indications for revascularization, options include percutaneous intervention, surgical bypass, or a combination (hybrid approach) of these. The choice depends upon the level of obstruction, severity of disease, the patient's risk for the intervention, and the goals for care. For patients with lesions that have anatomic features associated with durable clinical success with a percutaneous approach (single, short segment, uniform), guidelines suggest an initial attempt at percutaneous revascularization rather than initial surgical revascularization[18].

Open surgery procedure remains the method of choice for young patients, fit for surgery, with AID. The most common procedure in this setting is aortobifemoral (ABF) grafting that is associated with a 3% to 5% risk of operative mortality, relevant perioperative morbidity, and a delay in the return to normal routine[11]. Other open alternatives include axilobifemoral bypass and femoro-femoral bypass. Laparoscopic ABF for treating patients with advanced PAD has been established in dedicated centers [13].

Various techniques have been described for a successful endovascular revascularization of AID[21] (Figures 1,2). Although the mid- and long-term patency of the endovascular procedures and the ABF are comparable, the endovascular treatment option is preferred due to its minimally invasive nature and significantly lower peri-procedural morbidity[11, 12]. However, in case of unsuccessful endovascular treatment, atherosclerotic lesions not amenable for an endovascular procedure, or in young patients with acceptable risk of perioperative complications, open ABF is the preferred treatment option[11]. Endovascular treatment is preferably recommended for aortoiliac arterial injuries classified as type A, B and C in the TASC II classification[24, 25]. Primary patency rates of endovascular techniques were inferior to those of open revascularization, reinterventions could often be performed percutaneously and the secondary patency rates are comparable to surgical repair[44].

A recently approved National Institute for Health and Care Research (NIHR) funded UK-based randomised controlled trial (the EVOCC trial) comparing endovascular versus open management of AID is entering its pilot phase. This trial will be the first prospective trial of its kind in this anatomical area.

Among patients undergoing lower extremity revascularization, prevalent DM is an independent risk factor for major limb amputation and six-month hospital readmission[23]. Based upon the available data comparing outcomes in patients with and without DM, there does not appear to be any obvious subset of patients with DM for whom revascularization strategies should differ.

Performing prophylactic intervention, whether percutaneous or surgical, in patients with minimal

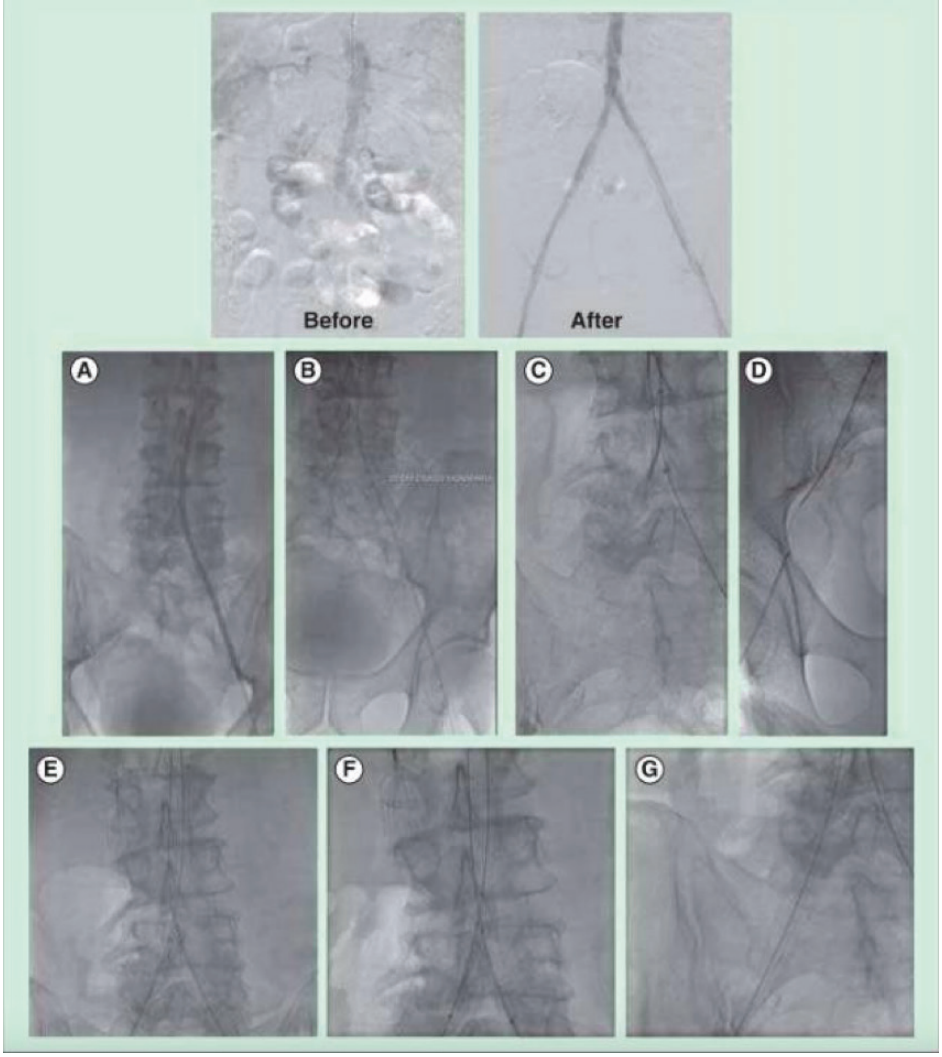

Figure 2

Endovascular intervention of patient with infrarenal aortic and iliac occlusions
(A) Initial flow channel with angioplasty balloon created after crossing lesion. (B) Lysis catheter in place through occlusion in aorta and left iliac artery. (C) Attempt at crossing right iliac occlusion by drilling wire and subsequent advancement of the sheath. (D) Snaring the wire after crossing the lesion to obtain brachial and femoral access. (E) Advancement of bilateral sheaths to the bifurcation. (F) Placement of an aortic and bilateral 'kissing' common iliac stents. (G) Treatment of remaining common and external iliac artery with self-expanding stents. At completion, the aorta and bilateral iliac arteries are patent without significant stenosis [1]

1 - Adpated from: Jm, G. CD, Beach. Strategies for managing aortoiliac occlusions: access, treatment and outcomes. Expert review of cardiovascular therapy. 2015;13(5).

claudication is not recommended. For those with significant or disabling symptoms of claudication unresponsive to lifestyle adjustment and pharmacologic therapy, intervention may be reasonable. For patients with chronic limb-threatening ischemia (eg, rest pain, ulceration), revascularization is a priority to improve arterial blood flow[26]. Some patients with acute thrombosis superimposed on chronic stenosis or occlusion (ie, acute-on-chronic ischemia) may benefit from thrombolytic therapy. For patients with chronic limb-threatening ischemia, the Society for Vascular Surgery (SVS) WIfI Classification is recommended to initially stage the limb and to assess the response to therapy. In the absence of limb-threatening ischemia, symptoms of PAD tend to remain stable with medical therapy[27].

Following revascularization, periodic clinical evaluation and postprocedure surveillance help identify problems that can contribute to loss of patency and potentially limb loss. The surveillance schedule depends on the type of intervention. Supervised exercise programs have been recommended as first line therapy for treatment of claudication. Exercise programs combined with risk factor modification offer the possibility of altering the clinical trajectory of PAD[29].

Management - Role of Medical Therapy

Studies regarding the role of medical therapy exclusively in AID are scarce. There are however several studies regarding PAD.

Recent observational studies confirmed that statins are effective and safe in both low and high-risk patients with PAD and offer additional benefits at high-intensity doses[31]. Although these studies differed in study design and sample composition, they arrived at similar conclusions comparable to findings from randomized controlled trials[31]. Also, in a subgroup analysis of a meta-analysis of 46 studies involving patients undergoing lower extremity revascularization, statins were associated with improved primary and secondary patency rates and significantly decreased amputation rates [32]. There is some evidence to suggest that the rate of restenosis/reocclusion following peripheral endovascular treatment is reduced with the use of antiplatelet drugs compared with placebo[33], but the available trials are small and of variable quality[34, 35, 36]. Guidelines and prescribing practices vary widely[34, 36, 37]. In the absence of high-quality data, the recommendations include prescribing aspirin (<325 mg/day) plus clopidogrel (75 mg/day) for one to three months, followed by lifelong aspirin. Based on data from the coronary literature, patients who receive a drug-eluting stent should receive clopidogrel for a longer period (3 to 12 months)[38].

Cardiovascular outcomes trials with two new classes of agents, the sodium- glucose co-transporter 2 inhibitors (SGLT2-i) and glucagon-like peptide-1 receptor agonists (GLP1-RA), have demonstrated reductions in cardiovascular events, including mortality, primarily for patients with DM and cardiovascular disease. In preclinical models, GLP1-RAs lowered vascular expression of proinflammatory pathways, improved endothelial function, and inhibited platelet aggregation and atherosclerosis.

Semaglutide and liraglutide are GLP-1 analogues. In patients with type 2 DM at high cardiovascular risk, semaglutide significantly reduced the rate of major adverse cardiovascular events (MACE) compared with placebo in the SUSTAIN 6 trial[39]. Data presented from subgroup analyses from LEADER (placebo-controlled trial of liraglutide) and SUSTAIN 6 have demonstrated reductions in cardiovascular events associated with GLP-1 analogues in patients with and without PAD[40]. With respect to limb-specific outcomes, treatment with liraglutide in patients with DM at high cardiovascular risk was associated with a significant reduction in diabetic foot ulcer-related amputations compared with placebo [41]. The STRIDE trial of 800 participants randomized to semaglutide versus placebo is underway to determine whether semaglutide has any benefits for walking ability in those with diabetes and PAD (clinicaltrials.gov: NCT04560998).

Cardiovascular outcomes trials for both SGLT2-i and GLP1-RA have included DM patients with PAD[42]. In patients with PAD at baseline, empaglifozin reduced cardiovascular death by 43%, all-cause mortality by 38%, and incident or worsening nephropathy by 46% versus placebo, consisting in patients without PAD[43].

CONCLUSION

AID remains a challenging area of PAD to treat. AID is frequently associated with multi-level disease and these patients commonly accumulate from significant comorbidities. Therefore, to further improve clinical and surgical outcomes, these preoperative geriatric prognostic factors will be of great importance and interest in vascular settings for both physicians and surgeons.

The literature on QoL for patients with advanced PAD is sparse, and especially, long-time follow-up studies assessing QoL and disease specific QoL are lacking. The evidence available on open and endovascular outcomes has often been of low quality due to small subject numbers and heterogeneity of presentations and interventions. From the patient's perspective, changes in the physical domains of a QoL tool after a treatment serve as a direct measure of the treatment effect.

Endovascular procedures offer significant advantages, including reduced invasiveness, lower complication rates, shorter hospital stays, and lower costs, with short-term outcomes comparable to open surgery. Conversely, open surgery boasts higher technical success rates and is not constrained by prior endovascular attempts. Consequently, there's a growing trend towards adopting an "endovascular-first" strategy for severe aortoiliac disease.

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