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Review article

Factors affecting suboptimal maturation of autogenous arteriovenous fistula in elderly patients with diabetes:A narrative review

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ABSTRACT

Autogenous arteriovenous fistula (AVF) is considered the preferred vascular access choice for individuals undergoing maintenance hemodialysis (MHD) and is widely utilized in China, as reported by the Dialysis Outcomes and Practice Patterns Study. Despite its popularity, the significant incidence of poor AVF maturation often leads to the need for central venous catheter insertion, increasing the risk of complications like superior vena cava stenosis and catheter-related infections, which in turn raises the overall mortality risk. With the prevalence of diabetes rising globally among the elderly and diabetic kidney disease being a leading cause of end-stage renal disease necessitating renal replacement therapy, our retrospective review aims to explore the various factors affecting AVF maturation in this specific patient population. While there have been numerous studies examining AVF complications in MHD patients, including issues like failure, patency loss, stenosis, thrombosis, poor maturation, and other influencing factors, there remains a gap in large-scale clinical studies focusing on the incidence and risk factors for immature AVF specifically in elderly diabetic patients. This paper delves into the pathophysiological mechanisms, diagnostic criteria, and unique considerations surrounding AVF maturation in elderly diabetic patients, distinguishing them from the general population. Our literature review reveals that elderly diabetic patients exhibit a higher risk of AVF immaturity compared to the general population. Additionally, there exists a continuing discourse regarding several aspects related to this group, including the choice of dialysis access, timing of AVF surgery, and surgical site selection. Furthermore, we delve into the management strategies for vascular access within this specific group with the goal of providing evidence-based guidance for the establishment and maintenance of functional vascular access in elderly diabetic patients.

1. Introduction

For patients undergoing maintenance hemodialysis (MHD), the autogenous arteriovenous fistula (AVF) remains the preferred

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vascular access. According to the Dialysis Outcomes and Practice Patterns Study, AVF accounts for a significant 88.2 % of vascular access utilization in China [1]. The maturation of AVF is an intricate process influenced by numerous variables. Studies conducted by Franco et al. [2]. revealed that as the utilization of AVF increases, the incidence of immature fistulas has risen from 23 % to 46 %. A meta-analysis by Bylsma et al. [3]., reviewing over 8000 studies, including 318, uncovered a concerning finding: only 26 % of fistulas were reported to be mature at 6 months, while 21 % were abandoned due to non-usage. Johannes W [4] and his team conducted a prospective cohort study investigating vascular access outcomes in octogenarian patients, discovering that the highest primary failure rate of AVF was observed in the elderly, reaching up to 42.1 % in this age group. Nadeau-Fredette AC [5]et al. reviewed 112 cases and found that 40 % of AVF in patients over 80 years old exhibited poor maturation. Furthermore, a retrospective study by Ghandour H et al. [6]., encompassing 401 AVFs, demonstrated that 40 % failed to mature even after surgical intervention. Qian JZ et al. [7]., in a retrospective study involving 22,000 patients over 77 years old, discovered that 55 % of AVFs required intervention due to maturation failure. Such failures often necessitate the placement of a central venous catheter for dialysis maintenance, which can lead to complications such as superior vena cava stenosis and catheter infections, thereby increasing the risk of all-cause mortality [8]. For effective hemodialysis, a functional arteriovenous access is paramount, and clinical guidelines generally recommend initiating AVF, albeit without considering specific patient characteristics.

Over the past three decades, there have been substantial shifts in patient characteristics. Diabetes mellitus, the fastest-growing contributor to chronic kidney disease (CKD) globally, has become a significant health concern. Among the elderly population, defined as those aged 65 and above, over a quarter have diabetes, and half have prediabetes. According to the findings of the research teamed by Yongze Li, a nationwide cross-sectional study conducted in China in 2019, approximately 33.5 million elderly individuals in China have diabetes. This figure represents one-quarter of the global elderly diabetic population. Notably, the prevalence of diabetes in individuals over 60 years old continues to increase with age, peaking after 70 years [9]. A large cross-sectional study in 2017 revealed that, based on the American Diabetes Association's 2018 diagnostic criteria, the prevalence of diabetes was 28.8 % in people aged 60–69 years and 31.8 % in those over 70, with a higher prevalence among women than men [10]. Among diabetic patients, the incidence of diabetic kidney disease (DKD) ranges from 20 to 50 %. Clinically, DKD is characterized by persistent albuminuria and/or a progressive decline in glomerular filtration rate (GFR), ultimately culminating in end-stage renal disease (ESRD). DKD is widely recognized as the most common cause of ESRD and renal replacement therapy (RRT). For instance, DKD-ESRD accounts for 28 % of RRT patients in the UK, 44 % in the US, and 38 % in Australia [11]. In mainland China, the number of DKD-ESRD patients was approximately 1.06 million in 2015, significantly outnumbering ESRD cases attributed to other factors [12].

However, despite research into factors such as failure, 5/10-year patency loss, stenosis, thrombosis, dysfunction, and immature maturation of AVFs among patients undergoing MHD, there is a dearth of large-scale clinical studies analyzing the incidence and specific risk factors for immature AVF maturation in elderly diabetic populations. Drawing from the available literature, our objective is to investigate and outline the pathophysiological processes and diagnostic guidelines relating to AVF maturation, focusing specifically on the distinct factors that influence AVF maturation in elderly diabetic individuals as opposed to the wider population. We also aim to explore various strategies for effectively managing vascular access in this specific demographic. Ultimately, our aim is to equip healthcare professionals with evidence-based insights to aid in the establishment and upkeep of well-functioning vascular accesses

Table 1
Keywords, inclusion and exclusion criteria formulated with the PICO strategy.

	Population	Intervention	Comparison	Result
Keywords	'Renal Failure, Chronic' or 'Chronic Renal Failure' or 'End-Stage Renal Disease' or 'Chronic Kidney Failure'AND 'Arteriovenous Fistula' AND 'elderly patients' AND 'diabetics'	–	'Renal Failure, Chronic' or 'Chronic Renal Failure' or 'End-Stage Renal Disease' or 'Chronic Kidney Failure' AND 'Arteriovenous Fistula'	'Primary failure' or 'Immaturity' or 'Poor maturation'
Searches	(1) 'Arteriovenous Fistula' (MeSH Terms) AND 'primary failure' AND 'elderly patients' AND 'diabetics'. (17) (2) 'Arteriovenous Fistula' (MeSH Terms) AND 'primary failure' AND 'elderly patients'. (86) (3) 'Arteriovenous Fistula' (MeSH Terms) AND 'primary failure' AND 'diabetics'. (26) (4) 'Arteriovenous Fistula' (MeSH Terms) AND 'primary failure'. (175) (5) 'Arteriovenous Fistula' (MeSH Terms) AND 'Immaturity'. (27) (6) 'Arteriovenous Fistula' (MeSH Terms) AND 'Poor maturation'. (17)			
Inclusion criteria	Patients with stage 5 CKD, who belonged to the geriatric and diabetics, underwent autologous AVF surgery.	To assess the maturity of autologous AVF within 3 months	Patients diagnosed with stage 5 CKD underwent autologous AVF surgery.	(1) Primary failure of autologous AVF. (2) Immaturity of autologous AVF. (3) Poor maturation of autologous AVF.
Exclusion criteria	Participants who are not involved in performing autologous AVF surgery, for instance, AVG procedures	Unpublished studies and topics unrelated to our criteria	–	The issue of patency loss after an autologous AVF for dialysis, such as stenosis and thrombus formation.

Note: For the section pertaining to the pathophysiological mechanisms and diagnostic criteria of AVF maturation, no specific study population was set. However, in the section exploring factors influencing AVF immaturity, a focus was placed on elderly or diabetic populations, considering demographic characteristics and certain biochemical indicators. Additionally, factors related to the vascular anatomy, such as radial artery diameter, cephalic vein diameter, and cephalic vein distensibility, were not limited to any specific population.

within this particular population group.

2. Methodology

2.1. Research objectives and question

The research question of this review has been conducted following the guidelines of the PICO strategy established by the National Institute for Health and Care Excellence. The PICO acronym consists of the following terms: population (P); intervention (I); comparison, control, or comparator (C); and result (O). Therefore, the research question aims to elucidate: “What are the specific influencing factors contributing to the immaturity of AVF in elderly diabetic patients compared to the general population? What are the considerations for managing vascular access in this specific group?"

2.2. Search strategy

A comprehensive search was conducted on PubMed, Scopus, and Embase from inception to July 1, 2024. Only peer-reviewed journal articles were considered for inclusion, excluding monographs, technical reports, or transcripts from scientific conferences. The search was guided by keywords formulated in accordance with the PICO framework (Table 1).

2.3. Inclusion and exclusion criteria

To guarantee unbiased research, the establishment of stringent inclusion and exclusion criteria was paramount. These criteria were formulated based on the PICO framework, as outlined in Table 1. This review encompassed articles with qualitative, quantitative, and mixed methodological designs.

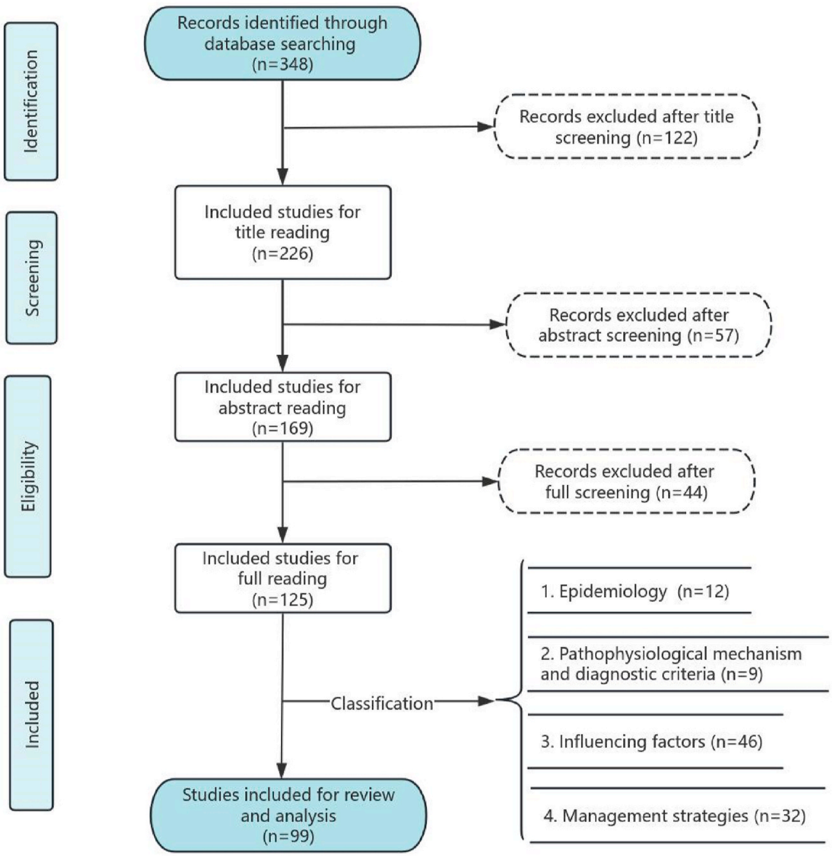

Fig. 1. Study selection procedure flowchart.
Source: Own elaboration

3. Result

3.1. Selection process

The selection process of the study encompassed multiple stages, involving the collaborative efforts of the authors (Fig. 1). In the initial phase of screening, titles of 348 articles were screened against the inclusion and exclusion criteria, resulting in the exclusion of 122 studies. Subsequently, abstracts of the remaining 226 studies were scrutinized, eliminating an additional 57 studies. This resulted in the identification of 169 articles for further analysis. In the subsequent selection phase, full-text reviews were conducted independently on the 125 studies, leading to the exclusion of 44 studies that did not adhere to the established criteria. Ultimately, a total of 99 articles were selected for detailed review and analysis.

3.2. The physiopathologic mechanism and criteria for a mature AVF

3.2.1. The physiopathologic mechanism

(1) Wall shear stress (WSS): The complex maturation process of an AVF fundamentally involves a sophisticated interplay of mechanical and biological phenomena, wherein numerous hemodynamic elements serve integral roles in governing its biological activities. Circulatory blood flow imparts two forms of mechanical forces on the vessel's structural integrity: shear stress - which is transversely transferred through interconnected endothelial cells, and WSS - a circular tensile force generated by the longitudinal impact on endothelial cells. A high WSS that falls within the physiological scope: Fosters endothelial cells to produce a higher ratio of vasodilating substances over constrictive ones, subsequently leading to vasodilation, inhibition of thrombus formation, and the impediment of migration and proliferation of medial smooth muscle cells converging on the intima. In a prospective observational study conducted by Cheng HS [13], it was observed that following surgery, the venous WSS significantly increased from a range of 1–6 dyn/cm^2 to a marked level of 10–70 dyn/cm^2, thereby approximating the magnitude encountered in the arterial system. In response to this elevated WSS, the vessel wall elicits resistance mechanisms and stress reactions, ultimately leading to compensatory vascular remodeling and vasodilation. This effectively maintains the original level of WSS, emblematic of a negative feedback regulation dynamic. Vascular rebuilding adopts two distinct modes: one is driven by an upsurge in deposition of neointimal cells, leading to inward reconstruction; while the other owes its origin to an increase in circumferential tension brought about by flow-mediated dilation, as opposed to merely increased pressure-resulting

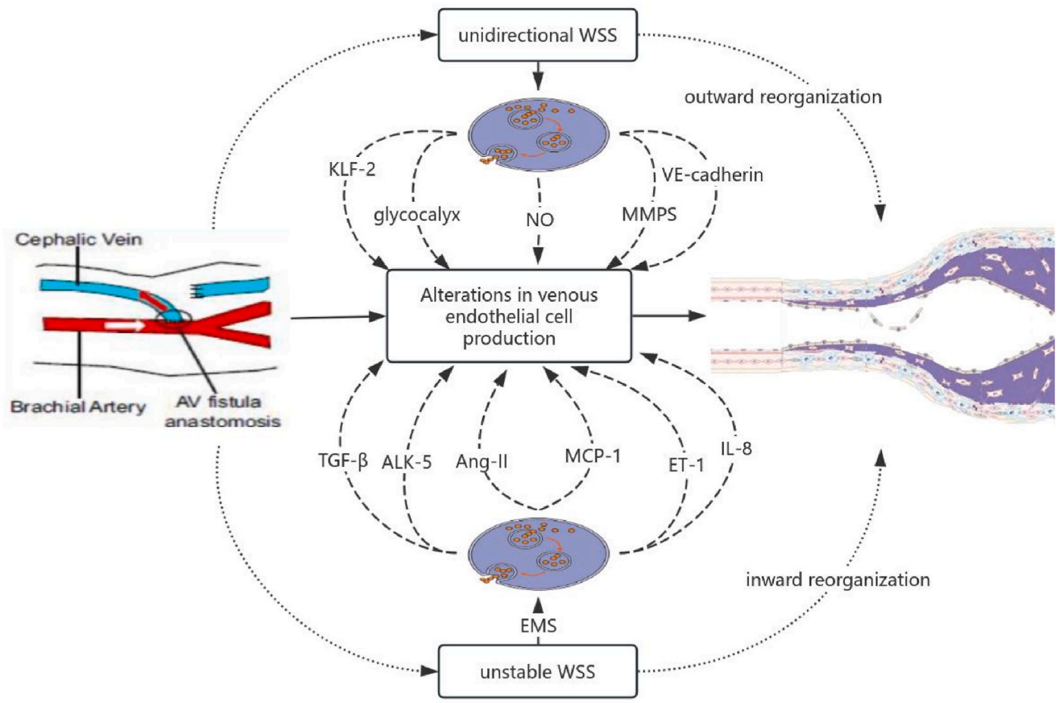

Fig. 2. Mechanisms of maturation of AVF endovascular fistulae.
Note: KLF-2: transcription factor Krüppel-like factor 2; NO: nitric oxide; MMPS: matrix metallo-proteinases; TGF-β: transforming growth factor β; ALK-5: activin receptor-like kinases-5; Ang-II: angiotensin II; MCP-1: monocyte chemotactic protein 1; ET-1: endothelin 1; IL-8: interleukin-8; WSS: wall shear stress; ECS: endothelial cells.

in outward reconstruction, thereby triggering eccentric intimal hypertrophy. The maturation process of AVFs relies heavily on the flow-induced response of vascular cells, particularly endothelial cells, which are capable of sensing an increase in WSS resulting from the diversion of arterial blood into the venous system. In instances where WSS shows high instability, characterized by rapid fluctuations in magnitude and direction typical of turbulent flow conditions, the vascular response may be compromised. This can potentially lead to cellular alterations, resulting in inward remodeling and suboptimal AVF maturation. WSS is considered a potentially crucial factor in the successful maturation of AVFs [14].

(2) In early-stage failed AVFs, the most prevalent issue revolves around luminal stenosis stemming from intimal hyperplasia (IH), ultimately culminating in thrombus formation. The pathogenesis of IH commences with endothelial cell injury and dysfunction, which triggers an inflammatory response, phenotypic switching, proliferation, and migration of smooth muscle cells, ultimately leading to vascular remodeling and matrix deposition, including calcification. A murine study revealed that CKD exacerbated endothelial dysfunction and neointimal formation [15,16]. Neointimal hyperplasia originates from the synergistic effects of inflammation, hypoxia, and hemodynamic WSS on vascular tissue [17]. Furthermore, the extracellular matrix (ECM) plays a pivotal role in vascular function. It provides structural and mechanical strength to the vessel, and communicates with vascular cells to regulate their differentiation and proliferation. Consequently, the ECM is intricately involved in the regulation of various processes during AVF maturation [18].

(3) While the molecular biological mechanisms initiating or advancing vascular maladaptation during the initial formation of AVF remain to be fully elucidated, numerous studies have firmly established a direct correlation between deficient AVF maturation and impaired vascular remodeling potential. A case-control study by Laisel Martinez [19]indicated that in patients grappling with sub-optimal maturation of AVF, preoperative concentrations of an array of cytokines – including granulocyte colony-stimulating factor (G-CSF), Interleukin-6 (IL-6), Myeloid Dendritic Cell (MDC), Regulated on activation, normal T cell expressed and secreted (RANTES), stromal cell-derived factor 1 alpha/beta (SDF-1a/b), transforming growth factor alpha (TGF-a), and thrombopoietin (TPO) – were markedly higher relative to the group comprising mature AVF. From this assortment, G-CSF, MDC, RANTES, SDF-1a/b, and TGF-a showed a significant association in a logistic regression analysis, thereby insinuating that elevated cytokine levels may potentially intensify the risk of a maturation debacle. These cytokines bear a close nexus with early inferior vascular remodeling. To exemplify, IL-6, possessing the capacity to activate endothelial cells and fibroblasts, as a consequence induces smooth muscle cell proliferation and migration while simultaneously fortifying immune cell infiltration. Various of cytokines and growth factors, such as platelet-derived growth factor, transforming growth factor-β (TGF-β), interleukin-1β, serve pivotal roles in the emergence of IH. Exploring the inhibition of individual growth factors and their signaling conduits constitutes an area of research focus for the prevention of IH post AVF surgery [20].

(4) Studies have demonstrated that the anastomotic angle affects the localized disturbed flow patterns, and selecting an optimal anastomotic angle for surgery can minimize the occurrence of IH due to the endothelial response to turbulent hemodynamics [21]. Fig. 2 for the mechanisms of AVF maturation.

When local flow conditions subject endothelial cells (ECs) to unidirectional WSS in arterial and venous AVF vessels, the cellular expression of KLF-2 and NO is anticipated to rise, leading to stable arterial and venous remodeling, along with augmented production of matrix metallo-proteinases, VE-cadherin, and glycocalyx on ECs. This, in turn, primarily results in an outward remodeling of the cephalic vein, ultimately leading to an increased luminal diameter and maturity of the AVF. Conversely, in scenarios where blood flow becomes locally unstable, characterized by disturbed and oscillating WSS and an unstable flow direction, ECs may enhance the production of transforming factors such as TGF-b, ALK-5, Ang-II, ET-1, IL-8, and MCP-1. As previously mentioned, these unstable flow patterns may also diminish the expression of KLF-2 and NO, thereby predominantly leading to an inward remodeling of the cephalic vein. This process can potentially cause AVF luminal narrowing, resulting in poor maturation.

3.2.2. Mature diagnostic criteria for AVF

(1) An ideally mature AVF encompasses:
① During dialysis, when the blood flow rate of the dialysis pump reaches 200–400 ml/min;
② The natural flow rate of the fistula achieves and sustains 800–1200 ml/min;
③ The vessels available for puncture are sufficiently elongated, positioned superficially, and easy to puncture;
④ High long-term patency rate and a low recirculation rate.

(2) International standards for AVF maturity:
① The 2018 European Society of Vascular Surgery Clinical Practice Guidelines explicitly state: When a fistula is formed, continuous flow from artery to vein triggers a series of changes, leading to alterations in vascular wall structure, WSS, and swift increase in blood flow within the initial 24 h. Most of the blood flow and augmentation in venous diameter are accomplished within 8 weeks. Post construction, an AVF is not immediately recommended for use. However, over time, these transformations render the fistula to become suitable for utilization - a process known as "maturation".
② According to the American Association for Dialysis Management, AVF maturity must be attainable for use four months post-surgery. AVF must satisfy the capacity for at least 8 instances per month, with a blood flow rate above 300 ml/min during hemodialysis.

(3) The criteria for AVF maturity in China:
① A physical examination reveals good tremors at the anastomosis, with no abnormal intensification, weakening or disappearance. The course of the venous segment of the fistula is straight, shallow, and easily accessible for puncture. It is uniform

in thickness providing ample area available for puncturing. The fistula vascular wall exhibits good elasticity, and palpable tremors are present with no amplified, diminished pulsations or disappearance.

② Clinical maturity refers to the ability of the fistula to be punctured during dialysis with a minimal risk of blood leakage. This implies that throughout the entire dialysis process, it can provide a surplus blood flow of no less than 250 ml/min, and can satisfy more than three hemodialysis treatments per week. Blood flow is considered insufficient when the pump-controlled blood flow does not reach 200 ml/min during dialysis.

③ Six weeks post-surgery, ultrasound maturation can be assessed. At this point, the natural AVF blood flow rate should be at least 500 mL/min. Additionally, the inner diameter of the puncture segment of the vein should be no less than 5 mm, and a skin depth should be no more than 6 mm.

④ The judgement standard for poor maturation of AVF: Failure to meet either clinical or ultrasound maturity standards. Specific attention should be given if maturity is not achieved six weeks post-surgery, as additional examinations may be necessary to ensure a timely diagnosis and treatment.

3.3. The influencing factors of AVF immaturity in the whole population

In fact, the maturation process of AVF is a multifactorial phenomenon, influenced by various factors that can be broadly classified into patient-specific and surgical-specific factors. Patient-specific factors encompass advanced female gender, the presence of conditions such as hypertension, previous instances of central venous catheterization, hypoalbuminemia, and overall poor vascular conditions. On the other hand, surgical-specific factors include the surgeon's technique and experience, the selection of an inappropriate surgical site, and premature puncture, all of which may contribute to delayed AVF maturation or even a complete failure of maturation. Additionally, there are several other factors that can impact the maturation process of AVFs. For a comprehensive overview of all factors influencing AVF maturation, kindly refer to Table 2.

3.3.1. Vascular conditions

(1) Vascular stenosis: Currently, there is no consensus on the minimum diameter of arteries and veins required to predict the maturation and patency rates of AVF. However, it is generally believed that the optimal diameter for AVF is greater than 2.0 mm for arteries and veins, with a minimum acceptable diameter of 1.5 mm for arteries. In a retrospective study conducted by Martinez-Mier G et al. involving 86 patients, demonstrated that venous diameters <2.15 mm and arterial diameters <2.95 mm significantly influenced the maturation and patency of AVF in the Mexican population [22]. Similarly, Mo H et al. performed a retrospective analysis on 45 patients who experienced early thrombosis of AVF and required salvage surgery. Their study found that venous stenosis was the most common cause of early thrombosis, and a minimum venous outflow diameter of ⩽2.5 mm was a significant risk factor for maturation failure [23]. Bashar K et al. [24]. concluded in a review that a cephalic vein diameter greater than 2.5 mm may serve as a better predictor of fistula maturation. Feng R et al. [25]. summarized in a systematic review that a cephalic vein diameter less than 2 mm negatively impacts the successful maturation rate of AVFs, thereby posing a

Table 2
Risk factors of AVF in elderly patients with diabetes.

Study	Setting	N	AV	Primary outcome	Risk factors
Drouven JW [4]	≥80 yo with diabetes	694	BC-AVF	Primary failure	Age, diabetes, hypertension, gender
Nguyen B [22]	The elderly	100	AVF	Primary failure	Age
Wan ZM [23]	Adults	353	RC-AVF	Immature AVF	Age, radial artery diameter
Arhuidese IJ [29]	Adults	381662	AVF	Decrease in maturation for diabetics	Diabetes
Alam F [30]	Adults	465	RC-AVF BC-AVF	Primary failure	Diabetes, female
Gan W [31]	Adults	236	AVF	Fistula maturation	Diabetes
Haque E [33]	Adults	197	AVF	Primary failure	Female, >65yo
Venkatnarayanan R [34]	Adults	197	AVF	Primary failure	Diabetes with≥3 antihypertensives
Yap YS [35]	Diabetes	233	AVF	Early failure of AVF	Female, lower hemoglobin level, prior peritoneal dialysis
Martinez-Mier G [42]	Adults	86	AVF	AVF maturation	Vein diameter<2.15 mm, Artery diameter <2.95 mm
Mo H [43]	Adults	45	RC-AVF BC-AVF	AVF maturation	Minimum venous outflow diameter ≤2.5 mm
Feng R [45]	Adults	1075	AVF	Functional maturation rate of AVF	Vein diameter <2 mm
Misskey J [47]	Adults	356	RC-AVF BC-AVF	Maturation failure	MVOD<3 mm and radial artery diameter <2.1 mm
Abrea R [48]	Adults	155	AVF	AVF maturation	Pulsatility index
Palmes D [76]	The elderly patients with diabetes	105	Perforating vein AVF, forearm AVF	Fistula maturation	Forearm AVF

Note: yo (year old); RC-AVF (Radio-cephalic arteriovenous fistula); BC-AVF (Brachial-cephalic arteriovenous fistula).

potential risk factor for AVF failure. Despite this, however, such risk can be significantly reduced by creating a middle cephalic vein fistula on the forearm of the same side following initial unsuccessful attempts [26]. Interestingly, a study conducted by Misskey J et al. [27] found that the combination of a radial artery diameter smaller than 2.1 mm and a minimum vein outflow diameter (MVOD) less than 3.0 mm acts as the most significant predictor of radio-cephalic AVF(RC-AVF) maturation failure and patency loss. A tiny radial artery diameter could lead to inadequate post-operative blood flow, unable to meet the requisite standards for fistula maturation, thereby escalating the incidence of maturation failure. Contrastingly, MVOD does not show any association with maturation. Abreu R et al. [28]. conducted a prospective study on 155 native AVFs, revealing that the failure to mature rate was 21.3 %. The pulsatility index emerges as a significant tool in predicting the failure to mature of native AVFs, serving as a novel hemodynamic variable.

3.3.2. Demographic characteristics

(1) Gender: In a retrospective observational study conducted by researchers including Li HL [29], encompassing 277 patients, it was found that female gender was associated with a failure in the maturation of AVF. The traditional belief holds that the vascular internal diameter in women is narrower than in men, which potentially leads to a more pronounced vascular response post-injury and diminished venous dilation capability, ultimately culminating in a lower fistula maturation rate [30]. In foundational experiments conducted by Kudze T and Cai CQ, an experimental AVF model in mice revealed a significant upregulation of fibrotic markers, including TGF-β1 and its receptors, in female subjects. This observation may indicate a correlation with impaired vascular remodeling and exacerbated endoluminal fibrosis [31,32]. A retrospective study conducted by Arhuidese et al. [33]. comprising 456,693 patients found no statistically significant difference in AVF maturity between genders. Interestingly, a retrospective study by Chan et al. [34]. encompassing 136 patients indicates that the fistula maturation rate does not exhibit any gender-specific influence among patients with a venous internal diameter exceeding 2.5 mm. This suggests that the participants in the studies may have had favorable vascular conditions, leading to no significant gender-related differences in AVF maturity.

(2) Blood pressure levels: Studies have illustrated that both high and low blood pressure levels can influence the maturation of an AVF. It was observed that lower preoperative and postoperative systolic, diastolic, and mean pressures were associated with early poor fistula maturation. Specifically, a postoperative systolic pressure ranging between 120 and 139 mmHg substantially reduced the incidence of fistula failure compared to a postoperative systolic pressure falling below 119 mmHg [35,36]. This phenomenon could be ascribed to the sluggish blood flow rate in patients with low blood pressure, which leads to inferior AVF blood flow post-surgery, weaker dilation effect on veins, and minimized WSS, thereby affecting vascular remodeling and fistula maturation adversely. In the case of patients with high blood pressure, endothelial injury results in a decrease in vasodilators and an infiltration of inflammatory cells, triggering intimal-medial hyperplasia, lumen narrowing, and an escalated risk of poor fistula maturation. However, to determine the optimal target blood pressure for patients, larger-scale research is necessitated [37].

(3) Obesity: The World Health Organization classifies Body mass index (BMI) of more than 30 as obesity. Notably, there has been an observed increase in kidney failure patients who are obese in recent years. Raulli SJ [38] conducted a retrospective study involving 611 patients and found a significant correlation between obesity and impaired AVF maturation. Arhuidese IJ et al. [39]. performed a retrospective study on 300,778 patients and observed that, upon sorting based on BMI, severe obesity was associated with a decreased fistula maturation rate. A systematic review by Lee SHT [40], encompassing 13 studies with a total of 305,037 patients, concurred with this viewpoint. Kim JK [41] conducted a retrospective study with 100 patients and discovered that the initial intra-operative blood flow (IOBF) in obese individuals was notably lower compared to non-obese patients. Further, he proposed an IOBF threshold of over 190 mL/min as a crucial indicator for predicting fistula maturation. This phenomenon could be potentially attributed to the deeper location of forearm vessels beneath the skin in obese individuals, where the excess adipose tissue augments the complexity of vein incision and hampers the achievement of the AVF maturation standard of a depth less than 6 mm from the skin. The surplus adipose tissue compresses subcutaneous vessels, culminating in deficient blood flow and thereby detrimentally affecting vascular remodeling and maturation. Nevertheless, Micah R. Chan's [42] research team, utilizing the dataset from the US Renal Data System DMMS Wave II, found no significant correlation between patient obesity and elevated fistula failure rates.

3.3.3. Analyzing biochemical indices impacting fistula maturation

(1) Hyperparathyroidism (Elevated PTH levels): Cheng Q [43]et al. in a prospective cohort study involving 819 patients demonstrated that elevations in serum PTH levels stimulate osteoblast activity and enhance the proliferation of bone-resorptive cells, ultimately leading to the release of calcium into the bloodstream. Additionally, Liu CT [44]et al. found in animal models that PTH amplifies the expression of the integrin B6 subunit in smooth muscle cells through the phosphorylated-Akt pathway, promoting the differentiation of these cells into myofibroblasts, thereby inducing vascular wall fibrosis. This series of events suggests an increased risk of fistula maturation failure with higher PTH levels. However, this pathway lacks sufficient clinical data to support its full implications.

(2) D-dimer: As an acute phase reactant protein, fibrinogen (FIB) exhibits elevated levels under conditions that trigger alterations in hemostasis, platelet aggregation, and the vascular wall. D-dimer, a primary degradation fragment of FIB, serves not only as evidence for acute thrombus formation but also as an indicator of persistent thrombotic conditions. Thrombogenesis is a crucial

factor contributing to the loss of AVF patency. Stolic RV [45]et al. conducted a revealing prospective cohort study with 81 AVF cases, tracking fistula survival within a year post-surgery, which suggested that FIB and D-dimer concentrations have significant predictive value for fistula survival. Complications resulting from fistula malfunction pose the highest risk within the first month after anastomosis creation, implying that fibrinogen degradation products (FDP) and D-dimer are likely key factors influencing the early maturation of AVF Akgül E [46] and others conducted a comprehensive retrospective cohort study involving 135 patients, categorized into mature and immature fistula groups within 2–3 months postoperatively. Their findings emphasized that elevated FDP concentration adversely impacts AVF maturation. Vascular stenosis and subsequent thrombosis, often secondary to stenosis, can trigger low blood flow and irregular vascular remodeling, which are common complications in cases of poor AVF maturation. Despite this robust evidence, the precise relationship between FDP/D-Dimer levels and poor AVF maturation remains to be conclusively explored. However, rigorous monitoring through frequent measurements of FDP/D-Dimer concentrations during the crucial three-month postoperative period addresses a crucial gap in identifying potential predictive factors for poor AVF maturation in high-risk patients.

(3) Wang Q [47] and colleagues demonstrated in a prospective cohort study involving 363 patients that preoperative cardiac index (CI) is associated with RC-AVF maturation. A decreased CI may serve as a potential predictor of an increased risk of fistula malfunction and a shorter primary patency time.

3.4. Factors affecting the maturation of AVF in elderly diabetic patients

Regarding the elderly diabetic population, large-scale data analysis has yet to identify definitive risk factors for impaired AVF maturation. However, aging and diabetes may adversely affect AVF maturation by influencing vascular integrity, albeit the outcomes remain inconclusive.

3.4.1. Regarding age

Nguyen B et al. conducted a prospective study over 2.5 years involving 100 elderly patients and identified a correlation between age and primary failure of AVF [48]. Additionally, Zi-Ming Wan et al.'s [49] cohort study indicated that age serves as a risk factor for impaired AVF maturation, with an over 1.54-fold increase in the risk of maturation impairment for every additional 20 years of age. This could be attributed to the gradual increase in the thickness of the intimal-medial membrane in vessels with age. Further complicating this issue, elderly individuals frequently display heightened risks of endothelial damage, narrowing, and blockage instigated by concurrent conditions like diabetes and peripheral vascular disease [50,51]. On the contrary, additional studies propose that the primary AVF patency rate does not bear a significant relation to age [52–54]. Therefore, the relationship between AVF success and age remains obfuscated, yielding no definitive conclusion.

3.4.2. About diabetes

In a retrospective cohort study encompassing 381,622 patients, Arhuidese IJ et al. [55]. observed a decreased maturity of AVFs in patients with diabetes, compared to those without. In a four-year prospective study conducted by Alam F et al. [56] involving 465 patients, it was observed that, after six months, 80 % of the fistulae achieved total patency, with a 20 % failure rate. Additionally, over 50 % of the patients, with half being females, were diagnosed with diabetes. Gan W et al. [57]. conducted a retrospective cohort study involving 236 patients and found that preoperative arterial and venous diameters, along with diabetes, are significant risk factors for AVF maturation. This finding may be attributed to the higher incidence of vascular calcification among diabetic patients with ESRD compared to non-diabetics, as well as the common occurrence of peripheral vascular pathologies such as atherosclerosis and narrowing. The calcification, thickening, and narrowing of the intima-media of vessels ultimately result in low postoperative blood flow, which do not favor vascular dilation and remodeling. Furthermore, an overabundance of glycation end products (AGEs) within the bodies of diabetic patients interacts with their respective receptors, precipitating vascular inflammation, fibrosis, and procoagulant responses. This cascade of events leads to vascular narrowing and endothelial dysfunction, thereby negatively affecting AVF maturation [58,59]. Remarkably, a prospective cohort study by Venkatnarayanan R et al. [60], comprising 197 patients, indicated that diabetes did not significantly contribute to primary AVF failure. However, diabetic patients taking three or more antihypertensives were a primary risk factor for such failure. Yap YS et al. [61]· conducted a retrospective study involving 223 patients diagnosed with ESRD concomitant with type II diabetic mellitus (T2DM). All participants had either an AVF or arteriovenous graft (AVG) as their primary vascular access. The study found that gender (specifically, females), a history of peritoneal dialysis, and reduced hemoglobin levels were significant factors contributing to an increased risk of premature vascular access failure.

3.4.3. About radial artery calcification

Arterial calcification is prevalent in 20–40 % of patients with ESRD, particularly among the elderly and those with diabetes. Vascular calcification poses a significant challenge to AVF dilation and remodeling, potentially compromising its maturation [62]. Ultrasound imaging can facilitate the identification and quantification of artery wall calcification; However, there is currently no standardized grading scale for upper limb arterial calcification. The guidelines set forth by the American Institute of Ultrasound in Medicine regarding vascular mapping only necessitate the identification and documentation of calcification, without any specified criteria for grading [63]. Literature on AVF in patients with extensive radial artery calcification remains sparse. Some studies reported that radial artery calcification might negatively impact AVF maturation, aligning with previous findings [64,65]. Nevertheless, some studies have reported no statistically significant difference in clinical and imaging based AVF maturity between mild calcification and controls, albeit with moderately reduced fistula blood flow [66]. A retrospective study involving 741 patients revealed arteriosclerosis in 100 of 166 diabetic patients, with only 16 cases (approximately 10 %) exhibiting immature AVF. This suggests that arteriosclerosis and plaque-related changes, particularly in T2DM, do not significantly hinder AVF maturation. Instead, the study underscores venous damage caused by repeated fluid a diabetic inistration in patients prior to dialysis as the primary impediment to AVF maturation [67]. Therefore, the impact of RAP calcification on AVF maturation requires further exploration in large-scale prospective studies.

3.5. Management strategies for AVF vascular access in elderly patients with diabetes

3.5.1. Preoperative evaluation and design for elderly patients with diabetes

(1) A comprehensive evaluation of patient status and dialysis access selection

The consensus recommendation advocates for patients possessing an estimated glomerular filtration rate (eGFR) of less than 30ml/(min·1.73 m^2) to be integrated into an ESRD management system [68]. In this intricate decision-making process of selecting the most suitable vascular access for each patient, one must effectively balance the intrinsic risks associated with vascular access surgery and the subsequent probability of successful AVF creation. Proficiency in the process of AVF creation, coupled with strategic application of ultrasound techniques during the preoperative stage, as well as during follow-ups, and the presence of pertinent technical expertise, collectively uphold the pillars of successful AVF creation [69].

The escalating trend of elderly diabetic patients transitioning to dialysis during Stage 5 CKD poses a significant healthcare challenge. These patients often encounter suboptimal vascular conditions, inadvertently augmenting the frequency of postoperative complications. Such complications encompass, but are not limited to, diminished patency periods, delayed maturation, and elevated primary failure rates. Consequently, the selection of an individualized dialysis access is paramount in enhancing the quality of life for dialysis patients. Research by Konner K [70] et al. in an observational study involving 748 patients revealed that AVF or catheter-based dialysis treatments are viable options for geriatric diabetic patients with limited life expectancy or other comorbidities. Kim H [71] et al. in a retrospective study of 41,989 patients demonstrated that for the elderly over 65, the AVF group exhibited superior primary, primary-assisted, and secondary patency rates compared to the elderly AVG group. Yan T [72] et al. conducted a literature review on vascular access (VA) in elderly hemodialysis patients, noting that patients over 75 may have higher frailty levels, increasing the complexity of vascular access selection due to a higher risk of vascular access complications and shorter life expectancy. A retrospective cohort study by Arhuidese IJ [73] encompassing 124,421 elderly patients showed that for surgically tolerable patients, AVFs remain the preferred modality for HD. For patients with a life expectancy exceeding a year, successfully established vascular access offers greater benefits than catheter-based dialysis. Specifically, AVF patients have a lower incidence of sepsis and mortality rate compared to transplant or catheter patients. However, it is crucial to note that AVF establishment is recommended 3–6 months prior to initiating HD therapy [74]. Palmes D [75] in a retrospective study involving 105 patients found that perforating vein AVF is superior to forearm AVF in elderly diabetic and hypertensive patients due to the proximal fistula location, likely attributed to improved artery distensibility during fistula maturation. Franco RP [76] et al. found AVG to be more advantageous for patients over 80. Additionally, Drouven J W [77] et al. in a prospective study involving 694 octogenarian patients supported the primary placement of a BC-AVF, achieving a low primary failure rate and significantly improved patency rates compared to other vascular accesses. Faaborg-Andersen CC [78] et al. found in a retrospective study involving 121 patients that systolic cardiac dysfunction is the most crucial nonmodifiable factor associated with unsuccessful AVF. Patients requiring hemodialysis with severe pre-existing cardiac dysfunction may not be suitable candidates for permanent access creation, and long-term catheter usage should be seriously considered as an alternative. Shingarev R [79] et al. in a retrospective analysis of a prospective computerized vascular access database revealed that the primary failure rate of fistulas is not influenced by the presence of an ipsilateral catheter. However, cumulative access survival is reduced in patients with prior ipsilateral catheters. Avoiding ipsilateral catheters may enhance long-term vascular access survival. A retrospective study by Buzzell M [80] et al. including 200 patients demonstrated that early postoperative follow-up for assessing fistula maturation is associated with a shorter time to the first successful cannulation of AVF for hemodialysis and a reduced time to catheter-free dialysis.

(2) Evaluation of vascular baseline conditions physical examination:
   ① Measurement of brachial artery blood pressure on both upper limbs. If the arterial differential is greater than 20 mmHg, it suggests inadequate arterial supply to the side with lower blood pressure, indicating possible proximal constriction.
   ② Allen's test: A positive result indicates subpar ulnar/radial artery perfusion to the extremity end. Creating an AVF at this juncture would increase the risk of postoperative limb ischemia.
   ③ Peripheral pulse sign: Compare the pressure along the course and on both sides of the brachial, radial, and ulnar arteries. A reduced or absent arterial pulse implies insufficient blood flow in the supplying artery.
(3) Ultrasonic assessment:
   ① Focused ultrasonic scanning of potential sites for AVF establishment is essential to detect any stenosis, calcification, or anatomical anomalies present in the upper extremity arteries. Although there is currently no explicit ideal ultrasonic standard for evaluating arterial calcification, we can assess its depth and expansibility after applying the tourniquet. Existing research suggests that patients with an appropriate radial artery diameter, relatively uniform color Doppler signal, and a Resistive Index up to 0.90 have a higher likelihood of successful AVF establishment and maturation.
   ② In relation to veins, it is crucial to take into account the internal diameter, orientation, depth, and expandability of the brachial vein bundle. When identifying a cephalic vein with a diameter of 2 mm, we can utilize its ability to dilate as an additional evaluation tool. If the dilation exceeds 2 mm, it can greatly improve the survival rate of the radial artery-AVF.

③ In establishing an AVF, we should prioritize veins with specific attributes including: a comparatively superficial location, ease of puncturing, substantial thickness, unobstructed and straight trajectory, uniform consistency, absence of pronounced narrowness, minimal collateral branches, good elasticity, and possible extensions above the elbow.
④ In deciding upon a surgical site, we adhere to the following general principles: favoring the upper limb over the lower; distal areas over proximal; the non-dominant side over the dominant; and considering limbs that have not had a central venous catheter placement.
⑤ As a principle, in elderly diabetic patients, the priority should be given to the establishment of RC-AVF. H Yasuhara's [81] evaluation of 287 AVFs demonstrates that revision is a reliable procedure for salvaging failed fistulas, achieving an acceptable patency rate regardless of the patient's risk factors for arteriosclerosis. It is noteworthy that forearm distal arteries in these patients are likely to exhibit severe atherosclerosis; thus, the precise criteria for selecting upper limb arteries and veins still requires further consensus [82,83].

3.5.2. *Considerations during surgery for elderly patients with diabetes [84]*

(1) Surgical procedure and precautions:
① It is crucial to avoid dissection of the venous sheath excessively, as overzealous stripping may potentially cultivate long-term stenosis of the fistula.
② The importance of proper management of venous tributaries and valves in a translocated AVF vein cannot be overstated. This is vital due to the potential for blood diversion caused by the presence of venous tributaries, which could lead to suboptimal blood flow within the fistula. Furthermore, this may result in an inordinately low WSS, which can interfere with the dilation and remodeling of the vessels. Also worth noting are actions of the venous valve, which potentially can instigate a series of vascular complications including IH restriction, episodic aneurysmal dilation, as well as thrombus formation. This cascade of events may disrupt the path towards the maturity of the AVF.
③ The alleviation of vascular spasms, a significant clinical concern, may be effectively facilitated by employing various therapeutic strategies. Methods include irrigating and dilating the vascular lumen to improve blood flow, as well as applying localized gentle pressure massages to the vessel to encourage vasodilation. Furthermore, immersing the affected vessel in a

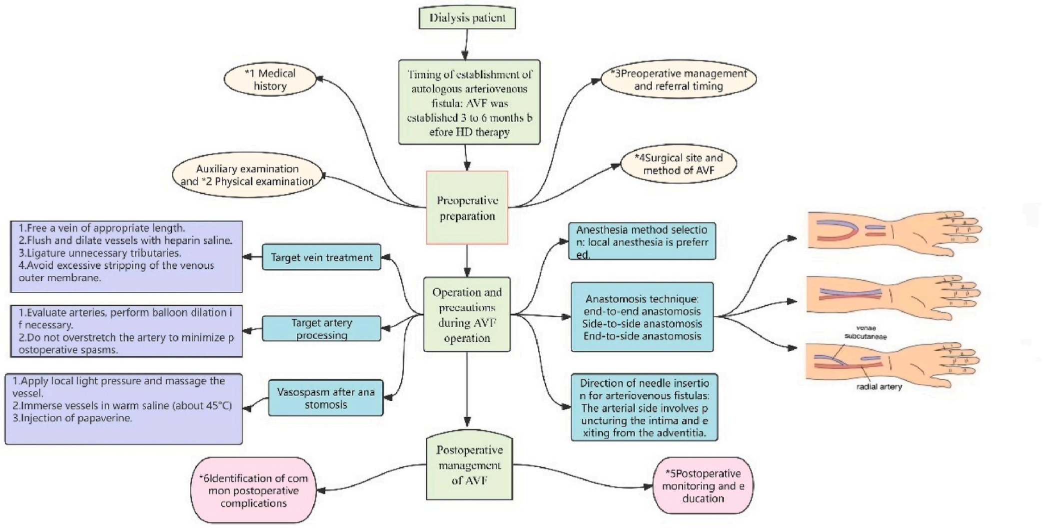

Fig. 3. Perioperative management strategy of the newly introduced AVF.
Note: *1. Primary diseases and accompanying conditions (Diabetes, Coronary Heart Disease and Heart Failure, Obesity, Malignant Tumors, Neurological Disorders, Skin Diseases); Arteries: Atherosclerosis, History of Arterial Puncture; Veins: Repeated Peripheral Vein Punctures, Infusion Catheter, Peripherally Inserted Central Catheters (PICC).
2.Arterial System Physical Examination: Understanding the pulse strength of the supplying arteries, comparing the arterial pressure differences in both upper limbs, performing the Allen Test; Venous System Physical Examination: There is significant individual variation in veins, so individualized evaluation is essential.
*3. ESRD Management: eGFR <30, inclusion in the ESRD management system; Vascular access knowledge dissemination, such as initiating functional exercises of the arm on the surgery side 4 weeks prior to surgery [85]; Referral to a physician who can establish hemodialysis vascular access should be done when eGFR drops below 15 ml/(min × 1.73 m^2) [86].
*4. favoring the upper limb, the distal areas, the non-dominant side, not had a central venous catheter placement.
*5PostAVFsurgery vascular monitoring; Dialysis scheduling and anticoagulants; Postoperative dressing changes and suture removal; Postoperative exercises; Physical rehabilitation therapy (Neuromuscular Electrical Stimulation, Far-Infrared Therapies).
*6Postoperative bleeding at the surgical site; Swelling of the limb on the operated side; Vascular Spasm; Thrombus Formation; Access-related Limb Ischemic Syndrome.

warm saline solution (around 45 °C) aids in vasorelaxation. Lastly, administering alkaline injections helps balance vascular pH levels, which in turn reduces spasms.

(2) Postoperative monitoring and assessment:

① After the surgical intervention, it is essential that professional nursing staff provide health education. In addition, an early initiation of AVF functional training should be considered to specifically address potential problems such as a narrow intravascular diameter and poor elasticity.

② The routine assessment of the patient's vascular patency is paramount. A pronounced tremor is palpable at the anastomotic site, extending along the venous pathway and progressively diminishing towards the cardiac region. During the anastomosis, a dual-phase, low-frequency, and continuous murmurmay be audible during both contraction and relaxation phases. The intensity of this murmur peaks at the anastomotic junction, gradually diminishing proximally, indicating optimal AVF function. In the event of a reduction or absence of palpable tremors, the emergence of pulsations, or are duction or disappearance of auscultated murmurs, accompanied by the appearance of high-pitched sounds, these often signify a possible narrowing or obstruction in the AVF, necessitating prompt investigation. Under certain circumstances, symptomatic treatment may be warranted, and a secondary surgical intervention may become imperative.

③ The evaluation of AVF maturity necessitates a comprehensive and systematic approach. The vascular access team should commence an in-depth investigation into the AVF's maturity two weeks post-surgery. Such evaluation encompasses inspecting the external appearance of the vascular pathway, delving into its internal structure, and calculating blood flow rates. This systematic approach significantly contributes to the swift identification and resolution of surgical complications that may arise, including limb swelling, operative site hemorrhage, vascular spasms, thrombosis formation, and limb ischemia syndrome. Thus, timely and suitable intervention measures can be promptly implemented. It is categorically imperative to abstain from performing precipitous punctures without meticulous investigation, in order to protect the continuity of blood vessel usage from unnecessary disturbances.

④ Interventionist measures should be adopted in accordance with individual circumstances to expedite the maturation of the intravascular fistula.The newly introduced AVF perioperative management strategy is depicted in Fig. 3 [84].

3.5.3. *Interventions to enhance AVFs maturation*

(1) Functional exercise:

Functional training, serving to boost hand blood circulation through the amplification of hand and forearm muscle contractions, emerges as an effective means to hasten AVFs maturation. Known for its safety, convenience, and cost-effectiveness, this method is widely adopted. At present, functional exercises can be bifurcated into hand exercise and hand combined with equal-distance arm exercise.

① In a randomized controlled trial, Krishna Kumar A/L S Katheraveloo's [87] research team demonstrated that hand exercises involving squeezing a ball for 30 min daily forming an empty or full fist, gripping onto a rubber ring, or using a hand grip strengthener, constitute viable ways to engage in productive hand training. Additionally, a systematic review conducted by Nantakool [88] found that upper limb exercise training positively influences the maturation of AVFs; these activities can indeed promote the clinical and ultrasonic maturation of AVFs. Nevertheless, a meta-analysis by S. Ramanarayanan et al. [89]. suggests that hand-grip training might only accelerate the clinical maturation of wrist AVFs, exerting limited influence on the ultrasonic maturation of wrist AVFs or both clinical and ultrasonic maturation of elbow AVFs.

② According to studies conducted by G. Distefano, L [90], and Tapia González et al. [91], the regime of hand combined with equal-distance arm exercise primarily suggests patients integrate ball-squeezing with joint movement (10 min per session, three times daily) 30 days prior to surgery or simply squeeze a rubber ball post-AVF surgery; rotate the wrist inward and extend it outward; lift obliquely a 1 kg heavy object to exercise the distal forearm; and stretch using an elastic band to apply pressure onto the proximal hand.

③ After a thorough review of the KDOQI Clinical Practice Guideline for Vascular Access: 2019 Update, we found significant global discrepancies in the implementation of postoperative functional exercises [91]. The type, commencement time, duration, frequency of these exercises, and whether they should involve blood flow restriction remain widely debated. Therefore, it is crucial to conduct in-depth future research for deriving conclusive evidence.

(2) Accelerating maturation through far-infrared radiation:

Far-infrared radiation is a form of electromagnetic wave with a wavelength range from 5.6 to 1000.0um. The application of a far-infrared therapy device on the limb with the fistula, carried out for 40 min per session three times a week, has been found to alleviate patient discomfort, minimize post-AVF surgical complications, and enhance the AVF's maturity. Importantly, this practice greatly improves AVF blood flow, thereby significantly elevating the rate of clinical maturation. Wan Q et al. [92]. conducted a meta-analysis including 21 eligible studies, which demonstrated that far-infrared therapy can substantially increase AVF blood flow, widen the vascular diameter, and decrease the occurrence of postoperative AVF complications such as stenosis and occlusion. However, precautions must be taken to ensure a safe distance between the device and the patient's skin during irradiation to avoid burn injuries.

(3) Medications:

① Anti-inflammatory drugs:

Inflammatory substances are known to activate multiple signaling pathways, including macrophage migration inhibitory factor, tumor necrosis factor-alpha, and TGF-β1. These activations contribute to endothelial dysfunction and the aggregation of inflammatory cells, which are linked to neointimal hyperplasia [93]. Atorvastatin, apart from its lipid-regulating effects, is recognized for its anti-inflammatory and antiplatelet aggregation properties. In one animal study featuring carotid artery-to-vein anastomosis, 108 mice were given atorvastatin daily via gavage seven days pre-surgery and 42 days post-surgery, with the test group receiving a higher dosage than the control group. The results indicated that atorvastatin noticeably reduces fibrin deposition, macrophage accumulation, and matrix metalloproteinase expression. Moreover, by impeding the activation, migration, and adhesion of inflammatory cells and decreasing the release of inflammatory mediators, atorvastatin can mitigate lipid peroxidation damage. Thus, it effectively safeguards the vascular endothelium and fosters fistula maturation [94].

② Anticoagulation and antiplatelet medications:

Following the establishment of an AVF, vascular endothelial damage, and changes in WSS can instigate platelet activation and thrombogenesis on the surface of the vascular endothelium. This process results in an amplified fibrinogenesis, thus promoting AVF occlusion. Statins, on the other hand, have the ability to enhance the expression of endothelial coagulation regulating proteins, curtail the production of thrombin and plasminogen activators, thereby mitigating microcirculatory stasis and obstructing thrombus development in AVF. A randomized controlled trial conducted by Viecelli AK [95] et al. involving 567 patients demonstrated that fish oil and low-dose aspirin administered for 3 months reduced intervention rates in newly created AVFs. Wahyudi W [96] et al. reviewed randomized controlled trials from Medline/Pubmed, EbscoHost, Embase, Proquest, Scopus, and Cochrane Central since 1987, with no language restrictions. Utilizing the Cochrane risk of bias tool 2, the study assessed bias risks and found that clopidogrel can reduce the incidence of primary AVF failure without significantly increasing bleeding events.

(4) Balloon-assisted AVF maturation:

In the modern clinical environment, endovascular interventions are progressively pivotal to AVF maturation and maintenance. The emergence of balloon-assisted maturation (BAM) technology has not only diminished AVF maturation time but also substantially improved its maturation rate. The efficacy of BAM in promoting AVF maturation can be attributed to several underlying mechanisms including, the intervention on non-stenotic healthy veins, application of balloon dilation to expand these veins, consistent application of arterial pressure on the venous wall to maintain AVF dilation. Furthermore, it averts any excessive and unnecessary endothelial damage, consequently shortening maturation time and enhancing AVF usage and functionality. A certain prospective randomized comparative study found the average AVF maturation times for the BAM and non-BAM groups to be 3.70 weeks and 5.91 weeks, respectively. A prospective randomized controlled trial conducted by Elkassaby M [97] et al. encompassing 300 patients revealed that 93.0 % of AVFs achieved functional maturation in the BAM group, with 78.3 % attaining early functional maturation within 2–4 weeks post-operation. Conversely, the non-BAM group had a final AVF maturation rate of 80.4 %, with only 32.2 % achieving early functional maturation. In a retrospective study involving 194 patients, Rizvi SA [98] et al. found that despite concerns from some researchers regarding BAM might potential to inflict damage to endothelial and smooth muscle cells (thereby increasing the incidence of restenosis via augmented smooth muscle cells and cytokine activation), BAM remains a recommended technique, particularly in cases where unexpected early treatments necessitate long-term dialysis. With the implementation of a series of interventions, most AVFs can effectively mature, thus buttressing AVF maturation efficiency, augmenting its patency, extending its lifespan, and elevating the quality of long-term dialysis treatment for patients.

3.5.4. Selection strategies and intervention guidelines for vascular access in elderly patients with diabetes

The selection strategy and intervention guidelines for vascular access in elderly diabetic patients have been extensively studied over the past two decades. However, due to the lack of randomized trials, standardized definitions for elderly patients, inconsistencies in criteria for AVF maturation, and a general lack of standardized definitions, the analysis of results has been limited. Therefore, most data are derived from retrospective observational studies with varying classifications based on age and VA placement, leading to conflicting outcomes and a lack of consensus on the preferred vascular access and location.

Nonetheless, a comprehensive assessment of the patient's medical history is paramount, particularly focusing on risk factors that may impact AVF development and long-term patency, such as hypertension, diabetes, obesity, and disorders of calcium-phosphate metabolism. These conditions often coexist with arteriosclerosis, calcification, and plaque formation. Prior procedures like coronary angiography, intravenous cannulation, placement of peripherally inserted central catheters, or other vascular interventions may cause venous endothelial damage and vascular narrowing. Furthermore, conditions like arteriosclerosis, stenosis, and endothelial injury can impede AVF remodeling and maturation.

Implementing targeted interventions to address these risk factors is crucial for minimizing the likelihood of poor fistula maturation. For hypertensive patients, maintaining stable blood pressure levels within an adequate range is essential. Postoperative hypotension or significant blood pressure fluctuations can lead to inadequate vascular dilation and adverse remodeling due to WSS. In elderly diabetic patients, a heightened emphasis should be placed on preventing hypoglycemia and managing blood sugar levels, rather than strictly controlling glycosylated hemoglobin indices. It is advisable to relax the target for glycosylated hemoglobin to below 8.0–8.5 % [99].

For patients with a history of venipuncture, precautionary measures should be taken to protect the arm's blood vessels prior to surgery, preventing preoperative venous damage from excessive venipuncture. Additionally, active lifestyle improvements, including a low-salt, low-fat diet, smoking cessation, alcohol moderation, and appropriate exercise, are recommended.

Based on the clinical studies reviewed and potential measures that may promote AVF maturation in elderly diabetic patients, we have summarized the overarching viewpoints and created a flowchart (Fig. 4). However, due to insufficient evidence, the flowchart serves as a reference only.

4. Conclusion

In conclusion, the development of AVF is influenced by a complex combination of various factors. These include, but are not limited to, the basic vascular conditions, patient demographic characteristics, specific biochemical indicators, and the implementation or lack thereof, of postoperative measures designed to promote fistula maturation. The impacts of vascular diameter and radial artery elasticity on fistula maturation have been firmly established both theoretically and in an expansive collection of clinical studies. However,

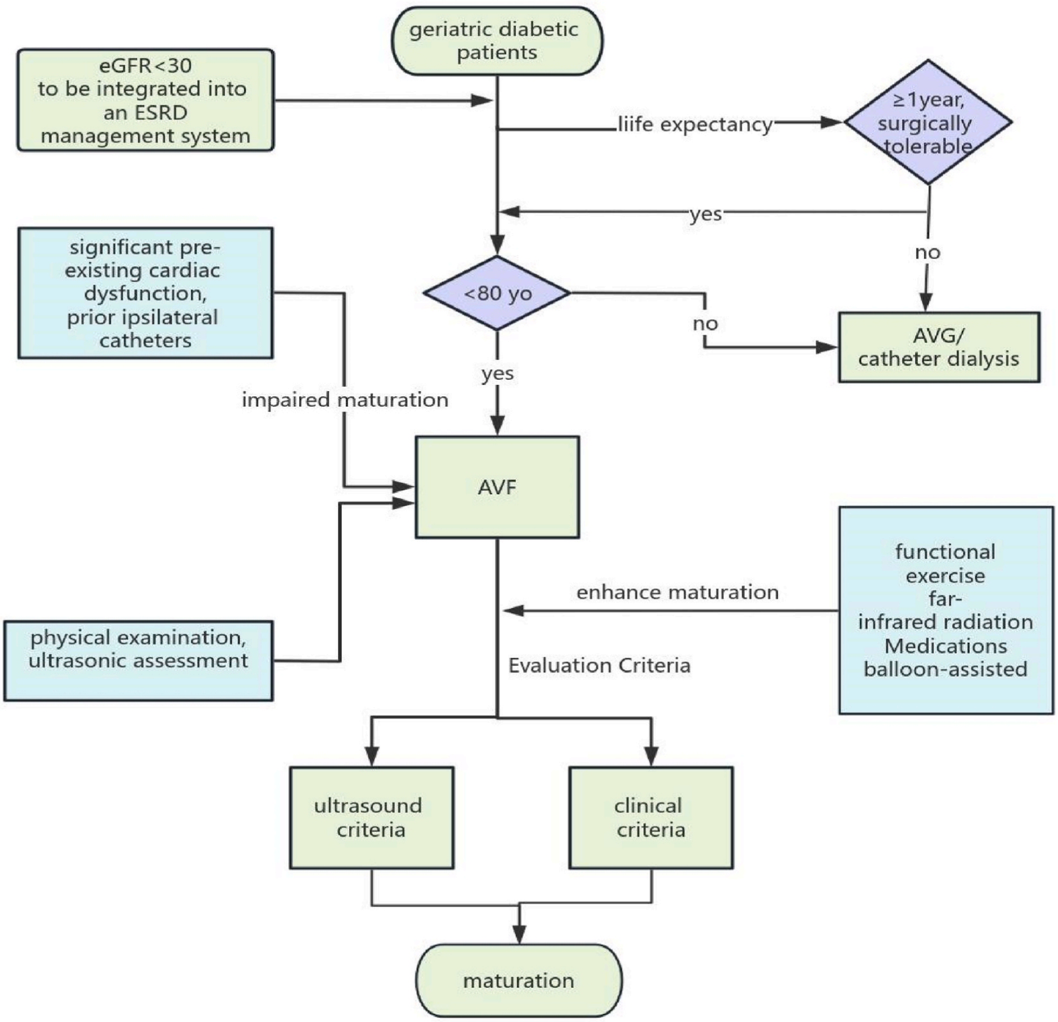

Fig. 4. The establishment and maintenance of AVF in the elderly patients with diabetes mellitus.

Note: When the estimated glomerular filtration rate declines below 30 ml/min, elderly diabetic patients are integrated into the end-stage renal disease management system. For patients over 80 years of age or with a predicted lifespan of less than one year, the selection of arteriovenous fistula (AVF) should be approached with utmost caution, favoring arteriovenous graft or catheter-based dialysis maintenance. For patients younger than 80, a comprehensive understanding of their underlying diseases and a thorough assessment of their vascular conditions is imperative. In instances where patients have a history of severe cardiac insufficiency, previous ipsilateral catheter dialysis, and ultrasonic findings indicative of petite radial artery and cephalic vein diameters, or radial artery calcification, these factors portend adverse AVF maturation and necessitate a cautious approach. Basic exercises, infrared therapy, medications, and balloon dilation may contribute to AVF maturation. Three months post-surgery, an evaluation of AVF maturity should commence, encompassing both ultrasonic and clinical maturity criteria.

it should be noted that the representation of diabetic patients aged over 65 years in these clinical trials is insufficient. The roles of demographic characteristics such as gender and hypertension, alongside biochemical parameters like hemoglobin, and PTH in fistula maturation are supported theoretically, with further empirical studies required to fully elucidate their mechanisms. Moreover, the consistency of these influencing factors' effects has yet to be conclusively determined across differing clinical study designs. Future research ought to specifically address the factors surrounding AVF maturation in elderly patients suffering from diabetes. This could be achieved by a comprehensive pre-operative assessment of the vascular condition of patients and selection of apt vascular access. Post-operative lifestyle modification guidance such as advice on functional exercise, smoking cessation, blood glucose regulation and blood pressure management would also be vital. By closely monitoring and assessing maturation and timely administering anti-inflammatory agents, we can potentially enhance the effectiveness and utilization rate of AVFs, thus ultimately establishing and maintaining a functional vascular access point for elderly patients diagnosed with diabetes to the greatest possible extent.

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Ethics committee approval was unnecessary for this review as it does not involve any research with human or animal subjects.

Data availability statement

Data is included in the text, and tables, and referenced in the article.

CRediT authorship contribution statement

Shuangyan Liu: Writing – original draft, Resources, Formal analysis, Data curation. **Yaqing Wang:** Writing – review & editing, Investigation, Formal analysis. **Xiaojie He:** Writing – review & editing, Investigation, Formal analysis. **Yuqing Wang:** Writing – review & editing, Investigation, Formal analysis. **Xiaodong Li:** Writing – review & editing, Supervision, Resources, Investigation.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

None If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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