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Research review

Vein graft adaptation and fistula maturation in the arterial environment

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ABSTRACT

Veins are exposed to the arterial environment during two common surgical procedures, creation of vein grafts and arteriovenous fistulae (AVF). In both cases, veins adapt to the arterial environment that is characterized by different hemodynamic conditions and increased oxygen tension compared with the venous environment. Successful venous adaptation to the arterial environment is critical for long-term success of the vein graft or AVF and, in both cases, is generally characterized by venous dilation and wall thickening. However, AVF are exposed to a high flow, high shear stress, low-pressure arterial environment and adapt mainly via outward dilation with less intimal thickening. Vein grafts are exposed to a moderate flow, moderate shear stress, high-pressure arterial environment and adapt mainly via increased wall thickening with less outward dilation. We review the data that describe these differences, as well as the underlying molecular mechanisms that mediate these processes. Despite extensive research, there are few differences in the molecular pathways that regulate cell proliferation and migration or matrix synthesis, secretion, or degradation currently identified between vein graft adaptation and AVF maturation that account for the different types of venous adaptation to arterial environments.

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1. Introduction

Vascular surgeons expose veins to the arterial environment during two common procedures, creation of vein grafts and arteriovenous fistulae (AVF). Adaptation of veins to the arterial environment, including the different hemodynamic conditions and increased oxygen tension, is characterized by venous wall dilation and thickening as an integration of the underlying processes of cellular migration and proliferation, as well as extracellular matrix deposition and remodeling. Successful venous adaptation is critical for long-term success of the vein graft or AVF, whereas unsuccessful adaptation,

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Table 1 – Basic characteristics of vein grafts compared with AVF.

	Vein graft	AVF
Preferred conduit?	Yes (bypass)	Yes (access)
Maturation in the arterial environment		
Outward remodeling	Yes	Yes
Wall thickening	Yes	Yes
1-y patency	60%–80%	50%–65%
Typical patient environment	Cardiovascular risk factors	Uremia/renal disease
Runoff	High resistance	Low resistance
Flow	Arterial	Supra-arterial
Pressure	High (arterial)	Low
Branches	Ligated	Patent
Vein left intact	No (reversed vein graft) Yes (*in situ* vein graft)	Yes
Surgical mobilization	Extensive	Minor (typical) Extensive (transposed)
Conduit diameter after remodeling	Medium	Large
Disturbed postsurgery	Undisturbed	Frequently cannulated

either insufficient or exuberant, may be a source of conduit failure that leads to patient morbidity and even mortality. Although our understanding of venous adaptation has substantially increased, this knowledge has not translated into successful therapy, and, accordingly, the failure rates of both vein grafts and AVF remain high, resulting in both patient suffering and significant health care expenditure [1,2].

AVF are the current optimal and preferred conduit for vascular access for hemodialysis. Compared with arteriovenous grafts and central venous catheters, AVF have the longest patency with fewest complications [3–6]. Despite their superiority among dialysis access choices, AVF still exhibit relatively high failure rates, as high as 60% failing to mature adequately to support hemodialysis in some reports [7,8], and primary patency rates of approximately 60%–65% within 1 y [9,10]. Similarly, vein grafts are the most commonly used and preferred vascular conduit for bypass surgery [11,12]. Like AVF, vein grafts also mature after surgical placement, a step thought to be necessary for long-term patency [13]. Vein grafts also have a significant rate of complications and failure, with 1-y primary patency rates reported to be as low as 60% [14–17]. Coronary artery vein grafts have higher patency rates, with 1-y patency rates of approximately 75%–90%, and 5- to 10-y patency rates >75% that decrease to 50% at ≥15 y [18–21]. The similarities and differences between AVF and vein grafts are summarized in Table 1.

The surgical formation of a vein graft or an AVF exposes the vein to the arterial environment of high blood flow and pressure that are typically considered injurious and that stimulate venous adaptation to the new environment [12]. This review compares both physiological and molecular adaptation of veins ("venous remodeling"), as either vein grafts ("vein graft adaptation") or AVF ("AVF maturation"), to this different environment, using literature specific to venous adaptation and not based on arterial data.

2. Surgical procedure

Several aspects of the surgical procedure are noteworthy and likely to affect venous remodeling. Vein grafts can be performed either in reversed, nonreversed, or *in situ* fashion, generally at the discretion of the surgeon. Reversed vein grafts create a flow environment in which the endothelial cells remain aligned to the direction of flow and the valves remain in their normal alignment, allowing antegrade flow with minimal resistance or disturbance. Nonreversed vein grafts are prepared similarly but require valve destruction, creating flow disturbance and even turbulence near the valve remnants; the endothelial cells remain aligned to the direction of flow but the flow direction is 180° reversed compared with the native venous flow. *In situ* vein grafts similarly require valve destruction and have reversed flow on the endothelial cells, but the veins are not removed from the native tissue bed, leaving the venous adventitia, as well as the vasa vasorum and nervous innervation, intact. Vein grafts, both reversed and nonreversed, require extensive handling and irrigation, resulting in spasm as well as endothelial damage and inflammation [22–24]. During coronary artery bypass, veins may be exposed to the colder environment of the bypass flow circuit and cardioplegia.

Similarly, AVF may be created directly or transposed from a deeper bed, although transposition in reversed configuration with valve destruction is distinctly less common. The AVF procedure is usually performed with less mobilization and surgical manipulation of the vein compared with vein grafts, resulting in AVF being performed more quickly and with less trauma, ischemia, and endothelial injury compared with vein grafts.

The systemic environment created by the comorbid conditions of the patient is often quite different between vein grafts and AVF. Vein grafts are typically created in patients with cardiovascular disease that is similarly frequently present in patients needing AVF. However, patients with AVF have advanced renal disease and uremia that is not present in many patients requiring vein grafts. Uremia is an independent factor that predisposes the AVF to failure to mature [25–28]. AVF are also cannulated for dialysis multiple times a week, unlike vein grafts that reside in atraumatic environments.

3. Flow and pressure

The minimum blood flow for hemodialysis in the United States is generally 350–450 mL/min, and to prevent venous collapse, the flow rate should exceed this minimum rate by at least 100 mL/min [29]. High flow rates correlate with successful access maturation, with 84% of fistulae with flows >500 mL/min eventually being adequate for dialysis, whereas only 43% of fistulas with flows <500 mL/min becoming adequate [29]. The National Kidney Foundation Clinical Practice Guidelines recommend a flow rate of 400–500 mL/min as a minimal threshold for re-evaluation of a fistula [30]. In Europe and Japan, however, hemodialysis is currently performed with lower flow rates but with longer sessions compared with those performed in the United States [31,32].

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