Histopathological Differences of the Pedicle Artery in Commonly Used Free Flaps: The Influence of Age, Gender, and Side

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Purpose: The increasing use of vascularized free flaps has increased the demand for a specified flap selection. This study investigated histologic differences in the arterial wall of the pedicle for commonly used free flaps and the effect of age, gender, and anatomic side on these differences.

Materials and Methods: Light microscopic examinations of vessel walls were performed on 245 specimens of the nourishing artery of commonly used free vascularized flaps in preserved cadavers. The peroneal artery (PA), radial artery (RA), inferior epigastric artery (IEA), deep circumflex iliac artery (DCIA), and circumflex scapular artery (CSA) were examined. Differences of histologic changes in the arterial wall and the effect of age, gender, and body side were investigated.

Results: All examined vessel specimens (age range, 62 to 98 yr; mean age, 83 yr; 15 female and 12 male) displayed mostly Class II changes. PA showed the greatest atherosclerotic changes, followed by the RA, IEA, DCIA, and CSA. Age had a meaningful effect on PA and RA. Anatomic side was important for PA and DCIA, whereas gender had a minor influence on vessel condition.

Conclusion: The vessel wall of different flaps showed different atherosclerotic changes depending on age, anatomic side, and gender. These differences should be considered in flap selection.

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The evolution and advancement of microsurgical techniques in reconstructive surgery have improved functional and esthetic outcomes.[1-4] However, the demand for fewer complications related to this type of surgery is increasing. New donor sites and increased surgical indications have produced a confusing and bewildering array of reconstructive options.[5-7]

Despite greater experience, failure rates should not be disregarded.[8] Often, failure is the result of a multitude of factors. Occlusion of nourishing vessels from thrombosis is an important cause and has been reported to be as high as 10 to 12%.[9-13] Atherosclerosis and endothelial damage can cause arterial thrombosis.[14,15] Population demographics for patients presenting with head and neck cancers have documented mainly elderly patients with a history of smoking and drinking habits and comorbidities such as vascular disease, diabetes mellitus, and hypertension.[16] The combination of these factors can give rise to a higher incidence of atherosclerotic changes. Vessels from various regions

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of the body differ in atherosclerotic changes.[17,18] However, there is a lack of clear information on the degree of histopathologic changes of the vessel wall in the pedicle of different flaps.[19-21]

This study examined the condition of the arterial wall of commonly used free flaps for histologic changes and the impact of age, gender, and anatomic side. The authors' hypothesis was that vessels from different donor regions would show different atherosclerotic changes.

Materials and Methods

After institutional approval, 270 vascular specimens were obtained from the left and right body sides of 27 preserved human cadavers. Any specimens that were not adequately prepared were excluded from the study. The specimens were taken by 2 maxillofacial surgeons and examined by 1 pathologist and 1 histologist who were blinded to the origin of the specimen. The following vessels were included in the study: peroneal artery (PA), radial artery (RA), inferior epigastric artery (IEA), deep circumflex iliac artery (DCIA), and circumflex scapular artery (CSA). Samples were fixed in paraffin and sections were stained with hematoxylin for light microscopic examination. Atherosclerotic changes of the vessel wall were examined under a light microscope. The condition of the vessel wall was evaluated according to the method of Stary et al[22] and divided into the following modified classes:

- Class 0, no pathologic change.
- Class I, slightly thickened intima with the beginning of filament degeneration in the media (Fig 1).
- Class II, thickened intima and progressive filament degeneration in the media (Fig 2).
- Class III, calcification and progressive plaque development (Fig 3).
- Class IV, florid plaques and necrosis (Fig 4).

STATISTICAL ANALYSIS

Data from the examination of specimens and the results were collected in an Excel table (Microsoft, Redmond, WA) and statistically analyzed with SAS 9.2 (SAS Institute, Cary, NC) in Windows 7 (Microsoft). There was no readjustment for the α value. The Fisher exact test was applied and P values less than or equal to .05 were considered statistically significant. The predictor variable was type of artery (DCIA, IEA, RA, AA, and PA), and the outcome variable was vessel wall condition. Other variables included age, gender, and side.

Results

Of the 270 specimens 245 (age range, 62 to 98 yr; mean age, 83 yrs; 15 female and 12 male) were evaluated for histologic changes. Histologic examinations showed some degree of atherosclerotic changes in the vessel wall (Fig 5). The CSA showed the fewest Class IV changes and most changes were Class II followed by Class III (Table 1, Figs 6-8). Although not significant, the CSA displayed a better condition compared with the RA (P = .447) and PA (P = .203), which was similar to the DCIA (P = .675) and IEA (P = .818). The DCIA showed all stages of atherosclerotic changes, but

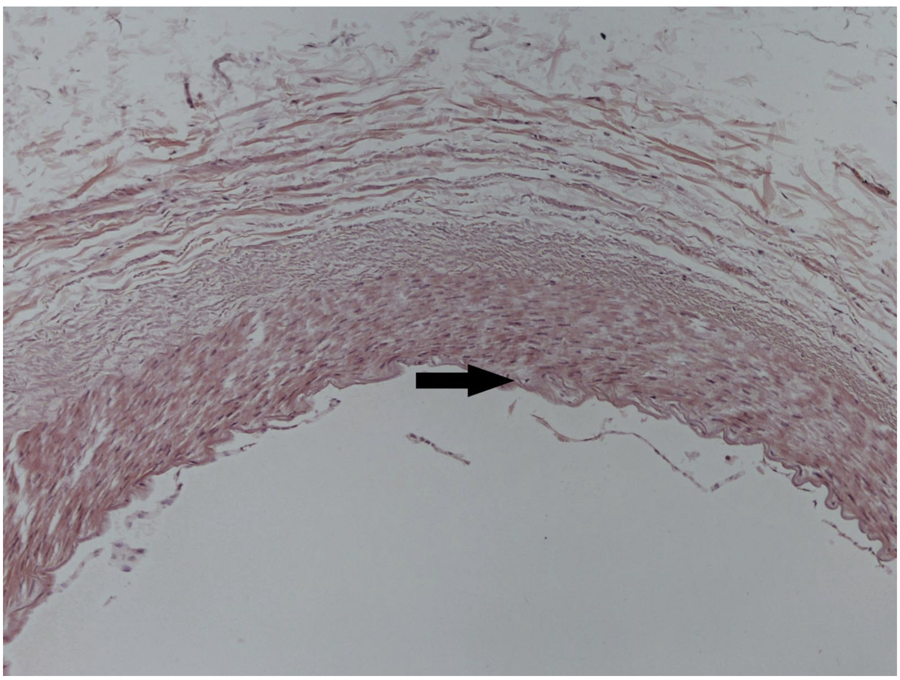

FIGURE 1. Light microscopic cross-section of the deep circumflex iliac artery with Class I changes (magnification, ×10). The slightly thickened intima (*arrow*) shows the initial degeneration of the filament in the media. The vascular condition of the vessel wall is still physiologic, with marginal changes in shape.

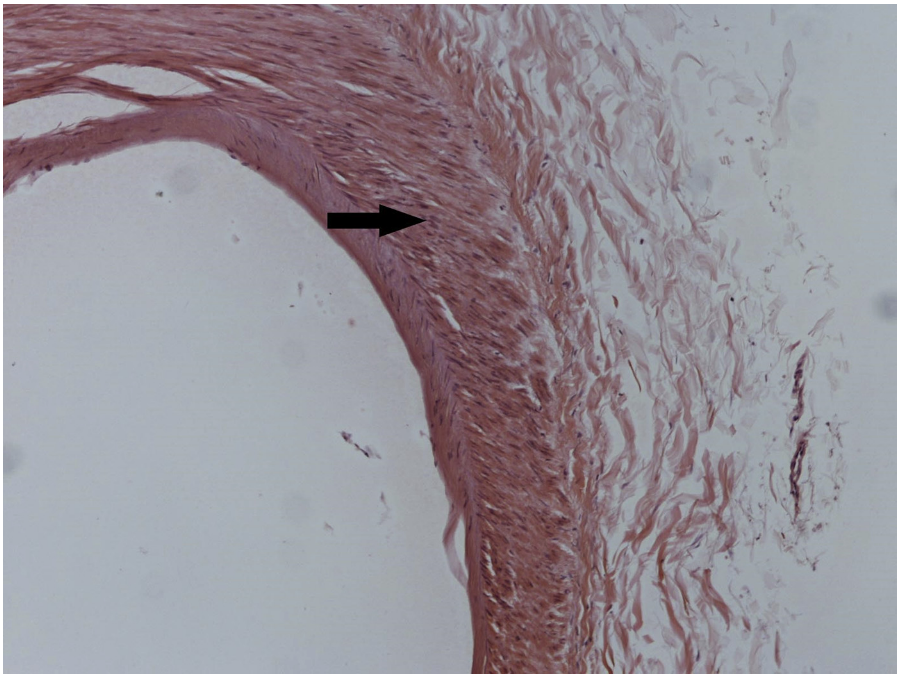

FIGURE 2. Light microscopic cross-section of the peroneal artery with Class II changes (magnification, ×10). The thickened intima shows progressive filament degeneration (*arrow*) in the media. There are visible pathologic changes between the intima and the media. However, the shape of the vessel is still normal.

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mostly Class II, followed by Classes III, IV, and I. The DCIA showed a significantly better condition compared with the RA (P = .001), PA (P = .026), and IEA (P = .027). Most changes seen in the IEA were Class III followed by Classes II and IV in addition to Class I changes in the male specimens. The condition

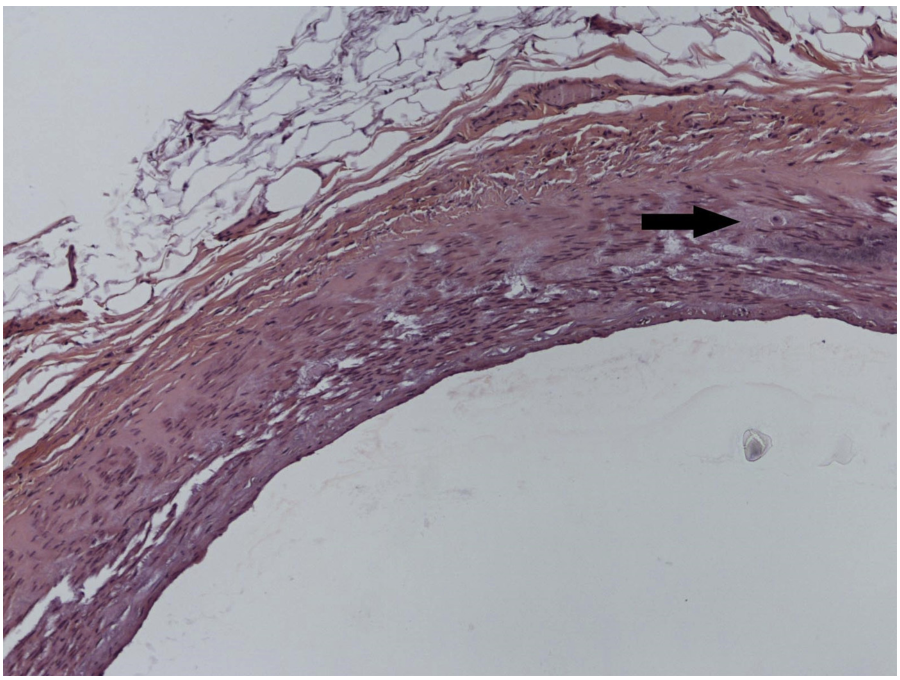

FIGURE 3. Light microscopic cross-section of the radial artery showing Class III changes (magnification, ×10). The thickened intima shows calcification in the media with ongoing plaque development (*arrow*). A palpable change of decreased vessel flexibility is observed.

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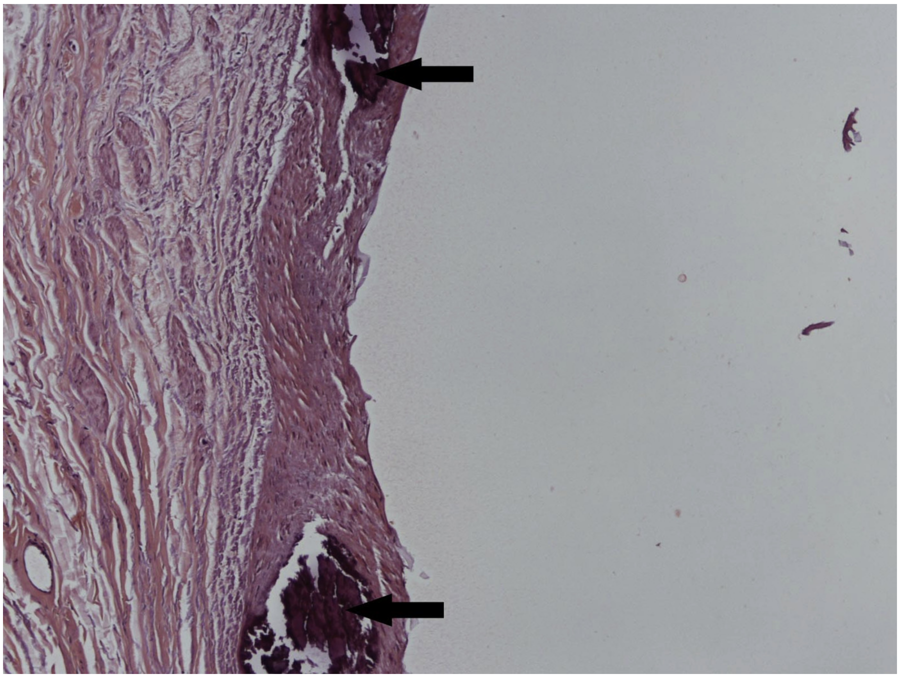

FIGURE 4. Light microscopic cross-section of the peroneal artery showing Class IV changes (magnification, ×10). A raised and damaged intima, florid plaques, and necrosis (*arrows*) in the media part are visible. The vessel shows a macroscopically severe change in shape.

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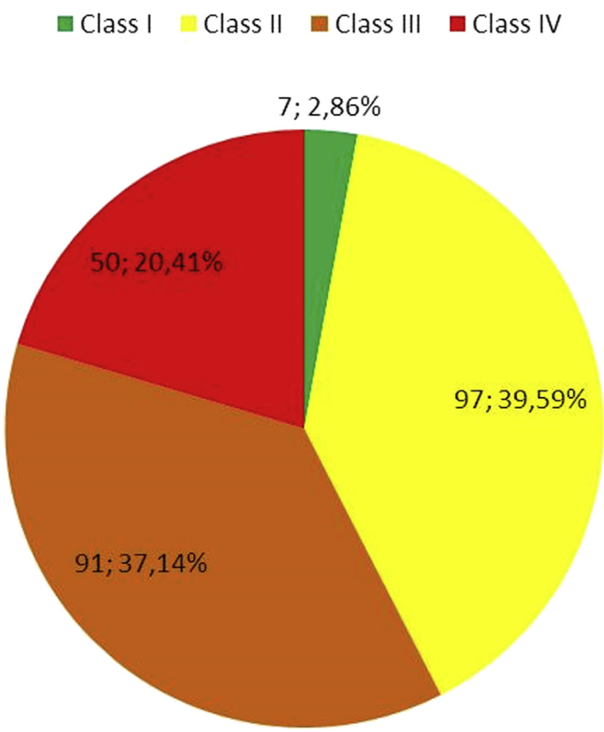

FIGURE 5. Results of histologic examinations of all flap feeding vessels. Class I, slightly thickened intima with the beginning of filament degeneration in the media; Class II, thickened intima and progressive filament degeneration in the media; Class III, calcification and progressive plaque development; Class IV, florid plaques and necrosis.

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of the IEA was significantly better than that of the RA (*P* = .012). The RA showed mostly Class III changes followed by Class II and IV changes; in female specimens, Class I changes were also seen. The condition of the RA was better than that of the PA (*P* = .110), but not significantly.

Age had a significant effect on the RA (*P* = .028) and PA (*P* = .018) and a nonsignificant impact on

Table 1. CHANGES IN VESSEL WALL FOR SPECIFIC VESSELS

Class	DCIA (n = 54)	IEA (n = 51)	RA (n = 50)	CSA (n = 46)	PA (n = 44)
0	—	—	—	—	—
I, % (n)	5.6 (3)	2 (1)	4 (2)	—	2.3 (1)
II, % (n)	51.9 (28)	29.4 (15)	30 (15)	56.6 (26)	29.5 (13)
III, % (n)	25.9 (14)	49 (25)	46 (23)	39.1 (18)	25 (11)
IV, % (n)	16.6 (9)	19.6 (10)	20 (10)	4.3 (2)	43.2 (19)

Abbreviations: Class I, slightly thickened intima with beginning of filament degeneration in the media; Class II, thickened intima and progressive filament degeneration in the media; Class III, calcification and progressive plaque development; Class IV, florid plaques and necrosis; CSA, circumflex scapular artery; DCIA, deep circumflex iliac artery; IEA, inferior epigastric artery; PA, peroneal artery; RA, radial artery.

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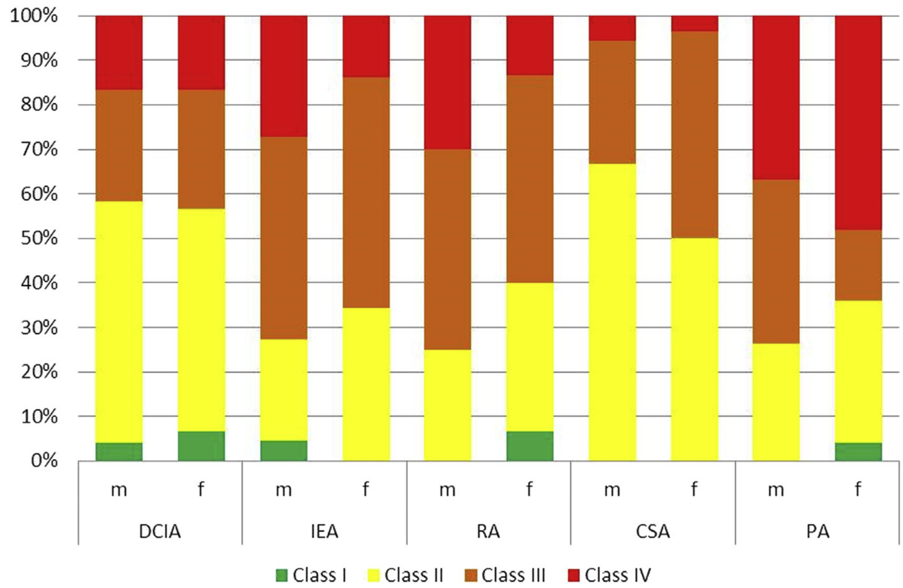

FIGURE 6. Gender-dependent atherosclerotic changes of flap vessels. Class I, slightly thickened intima with the beginning of filament degeneration in the media; Class II, thickened intima and progressive filament degeneration in the media; Class III, calcification and progressive plaque development; Class IV, florid plaques and necrosis; CSA, circumflex scapular artery; DCIA, deep circumflex iliac artery; f, female; IEA, inferior epigastric artery; m, male; PA, peroneal artery; RA, radial artery.

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the DCIA (P = .200), CSA (P = .207), and IEA (P = .937). Significant differences in vascular condition were observed for body side for the PA (P = .003), but were not significant for the DCIA (P = .31), RA (P = .068), IEA (P = .496), and CSA (P = .551; Figs 7, 8). Gender showed no significant differences among the examined vessels (PA, P = .375; IEA, P = .383; CSA, P = .448; RA, P = .468; DCIA, P = 1). Advanced age showed more Class IV changes (Fig 9). Mean values of changes of the examined vessels are listed in Table 2.

Discussion

The purpose of this study was to investigate histopathologic differences of the arterial wall of the pedicle originating from commonly used free flaps. In addition, the influence of age, gender, and anatomic side was examined. This should further refine the algorithm and selection for an appropriate flap. To address the research purpose, a cross-sectional experimental study was designed and implemented. The study population consisted of cadaver specimens. The authors

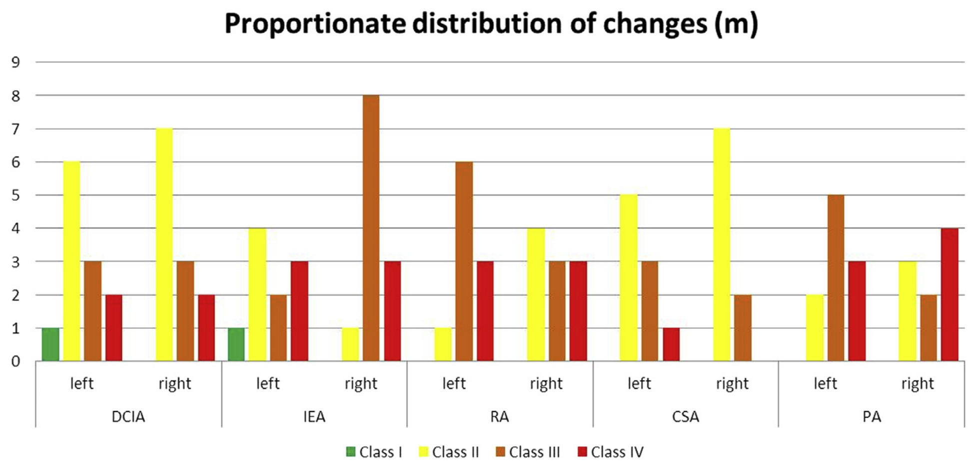

FIGURE 7. Results of histologic examinations of flap vessels in male specimens depending on anatomic side. Class I, slightly thickened intima with the beginning of filament degeneration in the media; Class II, thickened intima and progressive filament degeneration in the media; Class III, calcification and progressive plaque development; Class IV, florid plaques and necrosis; CSA, circumflex scapular artery; DCIA, deep circumflex iliac artery; IEA, inferior epigastric artery; m, male; PA, peroneal artery; RA, radial artery.

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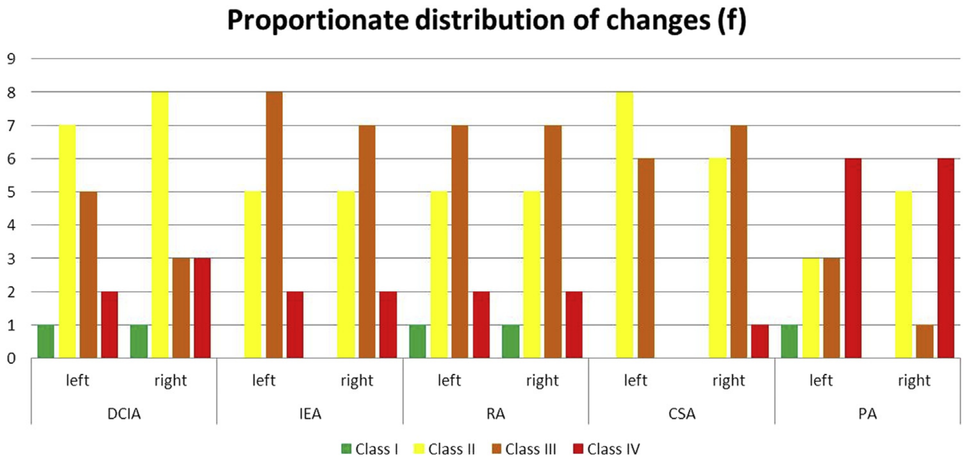

FIGURE 8. Results of histologic examinations of flap vessels in female specimens depending on anatomic side. Class I, slightly thickened intima with the beginning of filament degeneration in the media; Class II, thickened intima and progressive filament degeneration in the media; Class III, calcification and progressive plaque development; Class IV, florid plaques and necrosis; CSA, circumflex scapular artery; DCIA, deep circumflex iliac artery; f, female; IEA, inferior epigastric artery; PA, peroneal artery; RA, radial artery.

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examined 245 vascular specimens from different frequently used donor sides. Histopathologic changes were classified according to the method described by Stary et al,[22] but modified to simplify the comparison. Histologic examinations showed that all vessels examined in this study had undergone some degree of atherosclerotic change. Class I changes were seen in 2.86%, whereas Class II changes were seen in 39.59% (Fig. 5). The PA showed mostly Class IV changes (mean, female 3.08, male 3.11) followed by the RA (mean, female 2.67, male 3.05), IEA (mean, female 2.79, male 2.95), DCIA (mean, female 2.53, male 2.54), and CSA (mean, female 2.54, male 2.39). Although other studies have noted variability in atherosclerotic changes for different vessels, they used a different type of classification and did not consider the effects of age, gender, or body side.[21] In the present study, a significant effect of age was observed for the PA (P = .017) and RA (P = .028). The gender of the cadavers did not show any significant effect on the vessel wall, whereas anatomic side showed a significant effect on the PA (P = .003) and DCIA (P = .031).

Reconstruction of defects after oncologic resection of head and neck cancer is one of the most common indications for free flap surgery.[1-4,23] Head and neck cancer most commonly affects patients in the fifth to seventh decades of life. Given their advanced age, candidates often present with numerous comorbid medical conditions, such as systemic atherosclerosis.[24-27] The presence of atherosclerosis and some other mechanisms have been cited as a

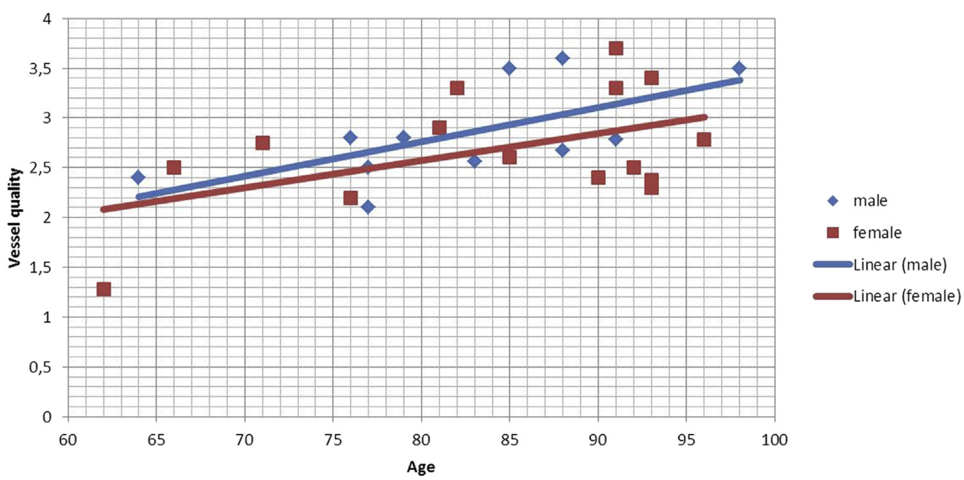

FIGURE 9. Continuous increase of atherosclerotic changes with advancing age.

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Table 2. MEAN CHANGES OF THE NOURISHING VESSEL OF DIFFERENT FLAPS

	DCIA	IEA	CSA	RA	PA
Female	2.53	2.79	2.54	2.67	3.08
Male	2.54	2.95	2.39	3.05	3.11

Abbreviations: CSA, circumflex scapular artery; DCIA, deep circumflex iliac artery; IEA, inferior epigastric artery; PA, peroneal artery; RA, radial artery.

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considerable risk factor for thrombosis and flap failure and subsequent complications.[28-36] In consequence, the selection of an alternative flap from a region with lower risks of atherosclerotic changes will decrease flap failure. In other words, even patients with peripheral vascular disease have a greater chance of a successful flap transfer if the right flap is selected. This assertion seems obvious; however, it has not been well substantiated by studies evaluating the viability of free flaps specifically in the setting of severe atherosclerosis. The present study showed that depending on the age, gender, and location of the vessels, there are different degrees of atherosclerotic changes. There was a strong dependency of the condition of the vessel wall with age and the region of flap origin. Moreover, some minor differences in regard to gender and anatomic side were observed, which should be considered in the clinical setting. Although maintaining the patency of a vascular anastomosis does not depend solely on the quality of recipient or donor vessels, selecting a flap from a region with a lower risk of atherosclerotic changes helps to increase flap survival. There is still no ideal prophylactic regimen that can completely eliminate the risk of thrombosis.[37,38]

The strength of this study is that all specimens originated from the same cadavers. However, greater access to the cadaver's medical history would have shed more light on this issue, but this information could not be obtained. A prospective study of a patient's medical history is not possible clinically or ethically, because it requires surgical approaches to all available flap regions in the same patient.

Age and anatomic side seemed to have an influence on vessel wall condition. Advanced age and other comorbidities should not preclude the use of microvascular free tissue transfers. Adequate preoperative planning and the selection of appropriate donor sites can help minimize flap failure.

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