Percutaneous intervention for infrainguinal occlusive disease in women: Equivalent outcomes despite increased severity of disease compared with men

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Objectives: **Experience with open surgical bypass suggests similar overall outcomes in women compared with men, but significantly increased risk of wound complications. Percutaneous treatment of lower extremity occlusive disease is therefore an attractive alternative in women, although it is not clear whether there is a difference in outcomes between women and men treated with this technique. We sought to determine the results and predictors of failure in women treated by percutaneous intervention.**
Methods: **Percutaneous infrainguinal revascularization was performed on 309 women between 2001 and 2006. Procedures, complications, demographics, comorbidities, and follow-up data were entered into a prospective database for review. Patency was assessed primarily by duplex ultrasonography. Outcomes were expressed by Kaplan-Meier curves and compared by log-rank analysis.**
Results: **A total of 447 percutaneous interventions performed in 309 women were analyzed and compared with 553 interventions in men. Mean age in women was 73.2 years; comorbidities included hypertension (HTN) (86%), diabetes melitus (DM) (58%), chronic renal insufficiency (CRI) (15%), hemodialysis (7%), hypercholesterolemia (52%), coronary artery disease (CAD) (42%), and tobacco use (47%). Indications in women included claudication (38.0%), rest pain (18.8%), and tissue loss (43.2%). Overall primary & secondary patency and limb-salvage rates for women were 38% ± 4%, 66% ± 3%, and 80% ± 4% at 24 months. In this patient sample, women were significantly more likely than men to present with limb-threatening ischemia (61.6% vs 47.3%, $P < 0.001$) and have lesions of TASC C and D severity (71.4% vs 61.7%, $P < .005$). However, there were no significant differences in primary and secondary patency rates or limb-salvage rates between genders. Furthermore, while women with limb-threat, diabetes, and advanced TASC severity lesions were at increased risk of failure overall, there were no differences between women and men with these characteristics.**
Conclusions: **Percutaneous infrainguinal revascularization is a very effective modality in women with lower extremity occlusive disease. Although women in this sample were more likely to present with limb-threat than men, patency and limb-salvage rates were equivalent between genders, even in high-risk subsets such as diabetics or those with lesions of increased TASC severity. (J Vasc Surg 2008;48:150-8.)**

Chronic lower extremity ischemia is a common manifestation of vascular disease that affects approximately 27 million persons in the United States and Western Europe and is associated with up to a 15-fold increase in mortality compared with those without evidence of peripheral vascular disease.[1-3] In many centers, the mainstay of therapy for chronic lower extremity ischemia has moved away from surgical bypass and toward less invasive endovascular treatment as a first line modality. As experience with endovascular techniques has grown, percutaneous intervention has been extended beyond the iliac circulation and into the infrainguinal locations. Furthermore, the factors which portend poor outcome after percutaneous intervention have begun to become more clearly defined.[4-8]

The effect of gender differences on outcome following percutaneous intervention is one area that remains to be further elucidated. Prior studies have documented the negative correlation between female gender and outcome following cardiac interventions, including both open surgical coronary revascularization and percutaneous transluminal interventions.[9-10] Substantial data has accumulated on the relationship between gender and peripheral vascular disease as well. There are numerous studies, for example, comparing the outcome following lower extremity bypass in men and women.[11-17] While these reports are at times conflicting, there appears to be a general consensus that men and women have similar patency and limb-salvage rates after open surgical bypass, and the primary difference between genders is an increased risk of wound complications in women.[18-19] The lower wound complication rate associ-

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Competition of interest: none.
Presented at the Twenty-second Annual Meeting of the Western Vascular Society, Kona, Hawaii, Sep 8-10, 2007.
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0741-5214/$34.00

doi:10.1016/j.jvs.2008.03.007

ated with endovascular therapy for lower extremity occlusive disease could reduce the frequency of these problems in women, although less data is available on endovascular therapy. There have been several publications pertaining to gender differences after endovascular treatment of the iliac circulation, and in these small series, female gender has been associated with reduced intermediate and long-term patency.[20-21]

Although infrainguinal interventions for lower extremity disease are becoming more commonly utilized, less has been reported regarding outcomes for interventions at these locations compared with the iliac circulation. In particular, gender differences and the effects of hormonal replacement therapy on infrainguinal interventions are largely unknown.

METHODS

Patients. Between the years 2001 and 2006, 309 women underwent 447 percutaneous interventions for infrainguinal lower extremity occlusive disease. These interventions were recorded in a prospectively maintained database and compared with interventions performed on 421 male patients over the same time period. All patients required intervention for chronic lower extremity ischemia and any patient requiring urgent or emergent intervention (open or percutaneous) for acute ischemia was excluded from analysis. This group of patients includes only those with isolated infrainguinal interventions, and patients undergoing simultaneous iliac interventions were excluded from analysis. Indications included debilitating claudication (defined as severely impairing lifestyle and ranging from 0.5 to 4 blocks) or limb-threatening ischemia (defined as rest pain, tissue loss or ulceration).

Demographic information, comorbidities, presence of hormone replacement therapy, operative details, and perioperative adverse events were determined by review of patient charts, operative reports and pre- and postoperative studies. Operative reports and angiograms were reviewed to determine lesion TransAtlantic InterSociety Consensus [TASC I] classification and location (femoral, popliteal, or tibial).[22] Postoperatively, patients were followed by physical exam and vascular lab evaluation. The divisional vascular lab database was reviewed to determine the results of pre- and postoperative noninvasive flow studies.

Procedures and imaging. Percutaneous interventions included angioplasty with or without stent placement, cryoplasty, and excisional atherectomy through either an antegrade or retrograde femoral artery access under local anesthesia with intravenous sedation. Procedures were performed either in an angio-equipped operating room using fixed fluoroscopic equipment (Siemens, Munich, Germany) or with a portable imaging fluoroscopic C-arm (OEC 9800; GE Medical Systems, Milwaukee, Wis). Iodinated contrast was used in patients with normal creatinine, and gadolium or combination gadolinium plus iodinated contrast was used in most patients with creatinine level greater that 1.3 mg/dl (use of gadolinium was determined by surgeon preference, and the majority of these cases were performed prior to the "black-box" warning regarding the potential link between gadolinium usage and nephrogenic fibrosing dermopathy [NFD]). All procedures were performed by members of the Division of Vascular Surgery, and type of procedure utilized was left to the discretion of the operating surgeon.

Technique. Selective angiography was performed to localize lesions and allow planning of interventions. Short 5-8F sheaths were used for antegrade punctures, and 6-8F Balkin sheaths (Cook, Bloomington, Ind) were used for retrograde punctures and contralateral interventions. Patients were systemically anticoagulated with intravenous heparin (100 units/kg) after sheath placement or before crossing critical lesions. Activating clotting time was maintained above 250 seconds for femoropopliteal procedures and above 300 seconds for tibial interventions. Lesions were crossed with either a luminal or subintimal technique using hydrophilic guide wires (0.035, 0.018, or 0.014 inch). Wires were supported using 4F or 5F angled glide catheters (Angiodynamics, Queensbury, NY) or Quick Cross catheters (Spectranetics, Colorado Springs, Colo). Re-entry into the luminal space beyond the lesion was confirmed by angiography before further intervention, and rarely were re-entry devices utilized. Balloon angioplasty was performed with appropriately sized noncompliant balloons with inflation times ranging from 60 to 180 seconds at 6 to 15 ATM of pressure. Stenting was performed selectively for >30% residual stenosis or flow limiting dissections. Excisional atherectomy was used as an alternative to balloon angioplasty in 292 (18.1%) of treated vessel locations, most commonly in the popliteal and tibial circulation. The Silverhawk atherectomy device (Fox Hollow Industries, Redwood City, Calif), which requires an 0.014 inch wire system, was used for all atherectomies. Pre- or postatherectomy adjunctive procedures including angioplasty or angioplasty/stenting were required in 40.9% of cases either to allow initial passage of the atherectomy device or to treat residual disease following atherectomy. Completion angiography with evaluation of the distal runoff was performed following interventions.

Aspirin was administered to all patients postoperatively unless contraindicated. For patients undergoing stent placement or atherectomy, a loading dose of Plavix 450 mg was administered in the post anaesthesia care unit, followed by 75 mg/day for 30 days.

Endpoints. Patency was determined by arterial duplex of the treated vessel and by ankle-brachial indices (ABI). Loss of patency was defined as occlusion or a velocity ratio of greater than 2.5:1 (representing a greater than 50% reduction in the lumen diameter) on arterial duplex or as a diminishment of >0.15 in the ABI. Routine follow-up was performed at 2 weeks postoperatively then at 6-month intervals, and included physical examination (pulses, wound healing, presence or absence of claudication or rest pain) and vascular lab assessment (ankle-brachial indices and arterial duplex ultrasound).

Statistical analysis. Demographic and comorbidity data was reported as mean ± standard deviation or as a

Table I. Demographics and comorbidities in men and women undergoing percutaneous infra-inguinal intervention

	Women *N (%)*	*Men* *N (%)*	P *value*
Total	309	421	
Age (y)	73.2	70.3	$P \leq .001$
Diabetes	177 (57.3%)	245 (58.2%)	ns
Chronic renal insufficiency	46 (14.9%)	114 (27.0%)	$P \leq .001$
End stage renal disease (HD)	21 (6.8%)	42 (10.0%)	ns
Hypertension	264 (85.4%)	352 (83.6%)	ns
Hypercholesterolemia	158 (51.1%)	263 (62.5%)	ns
Prior CABG	45 (14.6%)	119 (28.2%)	$P \leq .001$
Coronary artery disease	129 (41.7%)	245 (58.2%)	$P \leq .001$
History of MI	64 (20.7%)	134 (31.8%)	$P \leq .001$
Tobacco use	144 (46.6%)	238 (56.5%)	$P \leq .001$

Table II. Presentation and lesion distribution/Severity in primary interventions in men and women

	Women *(n = 371)*	*Men* *(n = 486)*	P *value*
Presentation			
Claudication	141 (38%)	255 (52.0%)	$P \leq .0001$
Limb-threat	230 (62%)	231 (47.3%)	
- Rest pain	70 (18.9%)	51 (10.5%)	
- Tissue loss	160 (43.1%)	180 (37.0%)	
TASC classification[a]			
TASC A & B	106 (28.6%)	186 (38.3%)	$P \leq .005$[b]
TASC C & D	265 (71.4%)	300 (61.7%)	
Most distal intervention			
Femoropoliteal	240 (64.7%)	327 (67.3%)	$P \geq .05$, ns
Tibial	131 (35.3%)	157 (32.3%)	

[a]For femoropopliteal lesions.
[b]For TASC A/B vs C/D.

percentage by patient (rather than by limb or intervention), while all treatment information, complications, patency rates, and other outcomes were reported by intervention. Univariate analysis of dichotomous variables between subgroups was performed by Fisher exact *t* test. Primary and secondary patency and limb salvage rates were assessed using Kaplan-Meier survival curves, and subgroups were compared by log-rank analysis to determine factors predictive of treatment failure. Multivariable analysis using Cox-PH modeling was performed to assess factors that were significant on univariate analysis.

RESULTS

Patients. Between 2001 and 2006, a total of 447 percutaneous lower extremity interventions were performed in 309 women, compared with 553 interventions performed in 421 men. Demographics and comorbidities of all patients stratified by gender are listed in Table I. Female patients were significantly older than the male patients (73 vs 70 years, $P < .0002$). The most common comorbidities for both men and women included hypertension, hypercholesterolemia, diabetes, coronary artery disease (CAD), and tobacco use. Chronic renal insufficiency (CRI), CAD, history of myocardial infarction (MI), and history of tobacco use were all significantly more common in men than women ($P < .001$ for each, see Table I.)

Indications and lesion distribution. For all procedures performed in women, 83.0% (371 interventions) were primary interventions, while the remaining 17.0% (76 interventions) were performed as secondary procedures on the same limb following re-stenosis or occlusion of the primary treatment site. Reintervention was less likely in men, who had 68 reinterventions and 485 primary interventions ($P = .04$), for an overall reintervention rate of 12.3%. Claudication was the indication in 38.0% of primary interventions in women, and in the remaining 62.0% the indication was limb-threatening ischemia. Women with limb-threat were further divided into those who underwent intervention for rest pain (30.4%) and those with gangrene or tissue loss (69.9%). In contrast, male patients underwent intervention for claudication in 52.7% of primary interventions, and presented with limb-threat to a lesser degree than the women (47.3% for men vs 62.0% for women, $P < .0001$, see Table II). In addition to presenting with limb-threatening ischemia more often, women were also more likely to have advanced TASC classification lesions. In this series, there was a preponderance of TASC B through D lesions and few TASC A lesions (5.8% overall) in either men or women. Women were significantly more likely to present with TASC C and D lesions than men (71.4% vs 61.7%, respectively, $P < .005$, see Table II). Reduced tibial outflow (<3 vessel tibial outflow) was also common, existing in 83.8% of women and 80.2% of men ($P > 0.05$, ns). Intervention was performed in the tibial location in 35.3% of women and in the femoropopliteal location in 64.7%. This treatment location distribution did not significantly vary between men and women. There were a total of 755 distinct lesions treated in women and 857 lesions in men. As displayed in Table III, the distribution of treated lesions and the use of different treatment modalities were similar between men and women. There was a trend toward increased use of angioplasty alone vs angioplasty with stenting in women compared with men, but this was not statistically significant ($P = .067$).

Outcomes. Thirty-day perioperative mortality was 0.5% overall and similar for women and men (0.7% and 0.4%, respectively, $P > .05$). Complication rates were equivalent between women and men, and included groin hematoma in 5.0% (requiring operative exploration in 0.8%), and pseudoaneurysm formation in 3.4% (all treated by thrombin injection) of all interventions. Renal dysfunction (increase in postoperative Cr by > 0.5 mg/dl) occurred in 2.0%, resulting in the need for hemodialysis in 0.3%.

Mean and median follow-up for all patients was 8.7 and 5.0 months, respectively. Primary and secondary patency rates (for all interventions) and limb-salvage rates (for patients with limb-threat) for men and women are illus-

Table III. Lesion distribution and treatment modality utilization

	Women	*Men*	*P value*
Lesion location			$P \geq .05$, ns
Femoral	44%	46%	
Popliteal	35%	34%	
Tibial	22%	20%	
Treatment modality			$P \geq .05$, ns
Angioplasty alone	43%	39%	
Angioplasty with stenting	37%	41%	
Atherectomy	20%	20%	

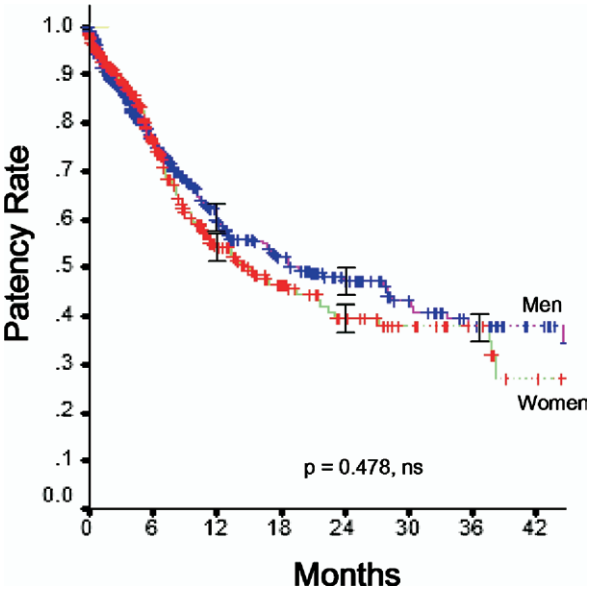

Fig 1. Primary patency rate for all interventions in women and men by Kaplan-Meier analysis. Women had 12- and 24-month primary patency rates of 54% ± 3% and 40% ± 4%, respectively, and primary patency did not vary for women and men.

trated by Kaplan-Meier curves and compared by log-rank analysis (Figs 1, 2, and 3). For women, primary patency rates at 12 and 24 months were 54% ± 3% and 39% ± 5%, respectively, while secondary patency rates were significantly higher at 75% ± 4% and 66% ± 4% ($P < .001$). Limb-salvage rates (in women with limb-threatening conditions) were 81% ± 3% and 80 ± 4%. Twelve- and 24-month primary patency rates for men were 59 ± 3% and 45% ± 5%, respectively, while secondary rates were 77% ± 3% and 66% ± 4%, respectively. Limb-salvage rates in men were 82% + 3% and 74% + 5% at 12 and 24 months. As shown in Figs 1, 2, and 3, there were no significant differences between primary and secondary patency or limb-salvage rates between men and women, despite the higher incidence of several important comorbidities in men.

Univariate log-rank analysis identified several factors associated with reduced primary patency in women undergoing percutaneous lower extremity revascularization (see

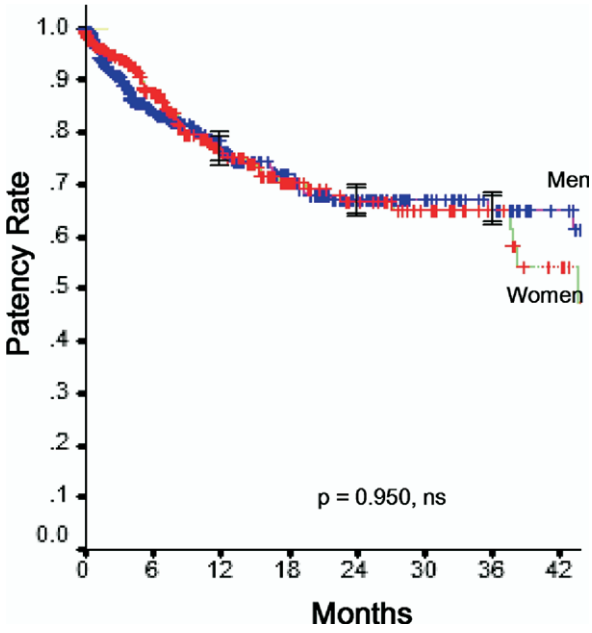

Fig 2. Secondary patency rate for all interventions did not differ significantly by gender. Women had 12- and 24-month secondary patency rates of 54% ± 3% and 40% ± 4%, respectively, while rates for men were 76% ± 3% and 67% ± 4%, respectively.

Fig 4, *A* and *B*). These included limb-threat as the presenting symptom or indication for intervention, lesions of TASC C & D severity, diabetes, and reduced tibial vessel runoff (<3 vessel). Limb-threat as the presenting symptom was the factor most strongly associated with reduced patency. Women undergoing percutaneous intervention who presented with limb-threat had a 1-year primary patency of 42% ± 3%, compared with women with claudication who had a patency rate of 67% ± 5%. Multivariate analysis confirmed that limb-threat as the indication for intervention ($P < .0001$), diabetes ($P < .03$), increasing TASC severity ($P < .05$), and reduced tibial runoff ($P < .05$) were each independently associated with reduced primary patency for both women and men. We found no significant differences in primary and secondary patency or limb-salvage for women compared with men when outcomes were stratified by the risk factors identified on multivariate analysis as well as all other proposed risk factors (see Fig 5, *A, B,* and *C*).

There were no significant differences in patency or limb-salvage between different treatment modalities (angioplasty alone, angioplasty with stenting, or atherectomy) when stratified by treatment location (femoral, popliteal, or tibial) for either women or men ($P > .05$, ns) on univariate analysis.

DISCUSSION

Recent data suggests that there are between 5 to 7 million persons in the United States alone with lower extremity occlusive disease.[23-24] Women have generally

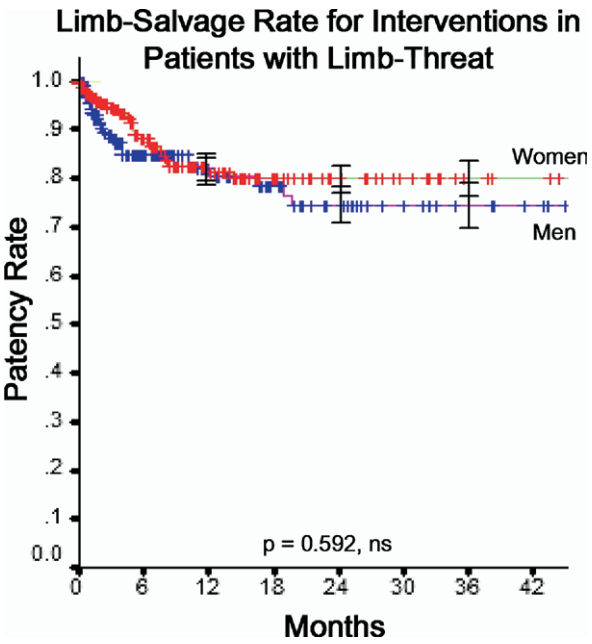

Fig 3. Limb-salvage rates (in women with limb-threatening conditions) were 81% ± 3% and 80% ± 4% at 12 and 24 months. These rates did not vary significantly for men and women.

been thought to have a lower prevalence of this disease process than men, and to some extent this may be true for young women before or early into menopause. While the reasons for this are not well understood, the mechanism may be related to an atheroprotective environment created by hormonal and metabolic factors that exist in premenopausal women. However, the incidence of lower extremity disease in women increases significantly after menopause and becomes at least equal to men in their sixth and seventh decades, reaching rates as high as 30% in octogenarians.[25-26] Several recent community-based surveys have even reported higher rates of lower extremity arterial disease in women compared with men.[27-28] Furthermore, several large studies have demonstrated the fact that increasing proportions of patients treated for lower extremity occlusive disease are women. In a large study of 5880 surgical reconstructions, Roddy et al found that the percentage of female patients treated at their institution increase from 15% to 37% over a 30-year period.[17] Similarly, Hultgren et al found that the proportion of female patients grew from 34% to 48% between 1970 and 1994 in a large trial from Sweden.[26] During the 5-year period of our study, interventions on women comprised nearly half the total number with 447 procedures.

Regardless of the true prevalence rate, multiple studies have shown that when women with lower extremity disease seek medical attention they have more advanced disease than men. In Eugster et al, women were significantly older (74 years vs 68 years, $P < .001$) and more likely to present with limb-threatening ischemia (81% vs 68%, $P = .013$).[29] Multiple studies have confirmed the finding that women are more likely to present with limb-threatening ischemia than men, a factor which generally is associated with a poorer outcome, and more likely to require amputation upon their initial presentation than men.[17,30-32] Similarly, women in the current study were significantly older than men (73.2 years vs 70.3 years, $P < .001$) and were more likely than men to present with limb-threat (62% vs 47%, $P < .0001$). Additionally, women were more likely than men to have lesions of increased complexity as demonstrated by the higher proportion of TASC C and D lesions in women than in men (71.4% vs 61.7%, respectively, $P < .005$). The reasons for this are likely multifactorial and may include social isolation, reduced access to care because of financial reasons, and confusion of symptoms of arterial disease with those of osteoporosis or arthritis, which are also prominent in this patient group.[33]

Intuitively, the more advanced disease at presentation displayed by women would seem to translate to poorer outcomes. From the limited available data pertaining to endovascular intervention in the iliac circulation, this may be true. There have been a few single institution studies that have demonstrated significant differences between men and women treated with percutaneous iliac interventions, with women having decreased immediate and long-term patency rates.[34] These differences were most evident in one study of women undergoing external iliac artery interventions; a fourfold increase in stent failure was observed in women relative to men.[35]

Despite these findings in iliac interventions, differential gender outcomes may not exist in the infrainguinal location. The majority of data pertaining to open surgical infrainguinal revascularization suggests that women fare as well as their male counterparts in terms of patency and limb-salvage rates.[11-13,17-18] The primary outcome differences between men and women undergoing infrainguinal bypass appear to be related to wound complications, cardiovascular events, and mortality, as evidence suggests that these may be higher in females patients.[11-12,19,36-37] As such, percutaneous infrainguinal therapy may be especially advantageous in women because of the fact that these types of perioperative complication rates are lower in catheter-based interventions than in open surgical bypass.

This publication represents the first study focusing on women with solely infrainguinal percutaneous interventions. A recent publication by Abando et al compared outcomes following iliac and infrainguinal interventions in men and women.[37] This study included 352 angioplasty procedures in 248 patients, including 173 interventions in women. One hundred and seventy-seven of the procedures were performed in the infrainguinal location, and when these were stratified by gender there was no difference in patency between men and women on multivariate analysis. Similarly, our current study showed no difference in primary patency, secondary patency, or limb-salvage rates between genders, even despite more advanced stages of disease in women upon presentation. Furthermore, unlike most reports regarding gender differences following open surgical infrainguinal revascularization, our study did not

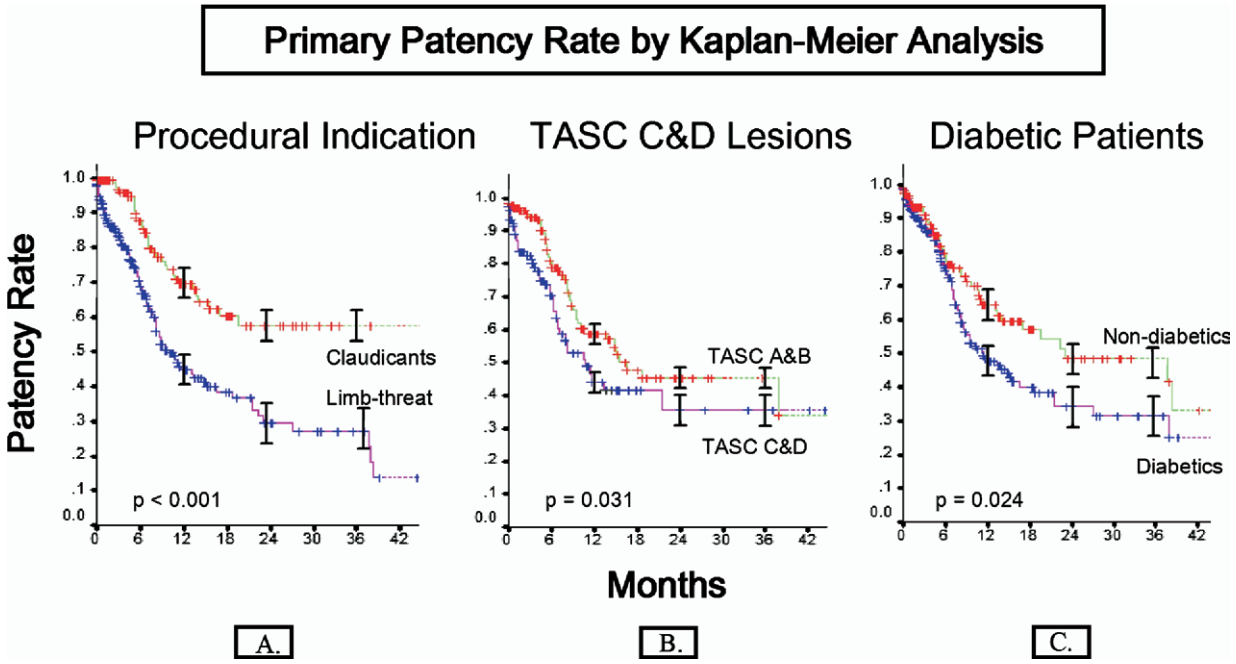

Fig 4. Univariate log-rank analysis revealed several factors associated with reduced primary patency in women undergoing percutaneous lower extremity intervention. These included (**A**) limb-threat as the presenting symptom, (**B**) TASC C & D lesion severity, and (**C**) diabetes.

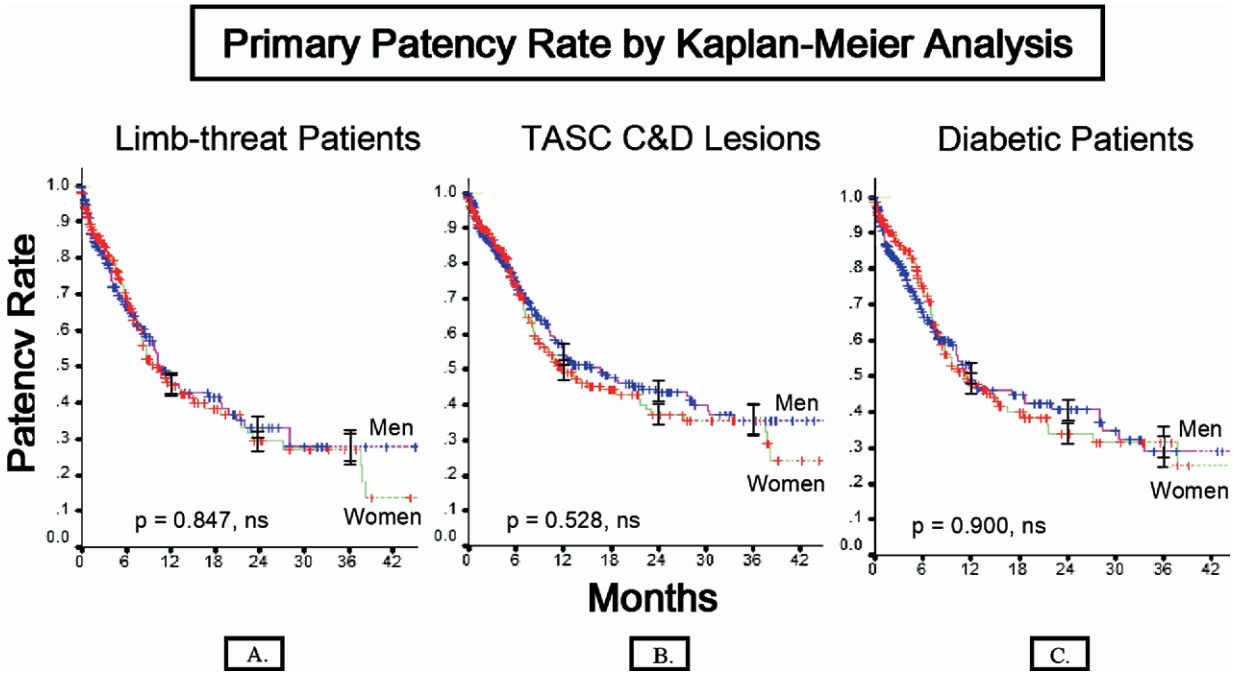

Fig 5. Even within high-risk subgroups, patency rates did not vary between men and women undergoing percutaneous infrainguinal revascularization.

show a difference in local wound complication rates or other perioperative events. Men and women did equally well and had acceptable complication rates following percutaneous intervention.

The reintervention rate is an important factor which may help explain the equivalent outcome across genders despite the increased likelihood of women to present with limb-threat and more severe TASC classification. Women

were shown to have a higher rate of reintervention on the same limb following the primary intervention than men (17.0% vs 12.3%, $P < .03$). This suggests that reintervention may be at least partially responsible for the sustained secondary patency and limb-salvage rates in women compared with men, although it would not impact the primary patency rate demonstrated here.

Because of the large sample size in this retrospective study, it was relatively well-powered for detecting a clinically significant difference in patency outcomes between men and women. On post-hoc power analysis, we found that the power of this study for the overall Kaplan-Meier curves for primary patency by gender at the 95% confidence level was 0.865. Because of the large number of interventions reported, the limit of detection for primary and secondary patency was well below the observed differences between genders at 12- and 24-month time points.

CONCLUSION

Percutaneous infrainguinal revascularization has evolved as an alternative to open surgical bypass with secondary patency rates of nearly 80% at 1 year. Although women tend to present with more severe infrainguinal occlusive disease than men, they appear to have equivalent patency and limb-salvage rates as men following percutaneous intervention. Furthermore, percutaneous intervention in women may be associated with fewer adverse perioperative events and wound complications than seen with open surgical bypass. Percutaneous lower extremity intervention can be considered a safe and effective first line modality in women with lower extremity occlusive disease.

The authors express their appreciation to Catherine J. Bresee (Department of Biostatistics, UCLA School of Public Health) for her assistance with the statistical analyses for this manuscript.

AUTHOR CONRIBUTIONS

Conception and design: BD, AV, JC, JK, PF, KK
Analysis and interpretation: BD, AV, SR, NA, JK, PF, KK
Data collection: BD, AV, SR, JC, PF, KK
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Final approval of the article: BD, AV, SR, JC, NA, JK, PF, KK
Statistical analysis: BD, AV, JC, PF, KK
Obtained funding: KK
Overall responsibility: BD, AV, KK

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Submitted Sep 19, 2007; accepted Mar 3, 2008.

DISCUSSION

Dr Tej Singh (*Sunnyvale, Calif*). Good morning. President Ballard, officers, members and guests of the Western Vascular Society, I wanted to thank you for the opportunity to discuss Dr. DeRubertis' well-written and concise manuscript regarding endovascular outcomes for infrainguinal occlusive disease in women compared with men.

There is no doubt that the content of the study and the topic in general causes significant discussion and distress at times in our vascular surgical community. At every hospital in America, endovascular infrainguinal interventions with new technologies are happening at a rapidly growing rate, even though the indications, long-term follow-up and consistent results are still not clear. We all recognize that rapid growth in these procedures does have some important clinical advantages in appropriately selected patients. Selection and patient referral patterns may dictate care in many centers unfortunately.

Dr DeRubertis and his vascular surgery group have described in this paper their excellent results and clinical follow-up of a large number of interventional procedures for lower extremity occlusive disease in both sexes. As he described in his presentation, women have equivalent outcomes compared with men even though they may have more advanced disease, increased task severity, and unknown hormonal effects. This is promising when we all recognize that some women may have poor surgical options and also tend to have smaller diameter distal targets making surgical options difficult technically and with known complications. While it is promising that women and men have equivalent outcomes based on the study and without necessary randomized trials, I would caution the reader and the listener from going out and purchasing arthrectomy and crossing devices for all patients with chronic limb ischemia. The primary patency of 40%, secondary patency and 60%, and limb salvage of 80% at 3 years has been reported in other experienced centers but may not reflect the results in all clinical practices which I believe may unfortunately be less.

To stimulate discussion, I have three very important questions for you.

(1) Approximately 22% of the women in the study had chronic renal failure or were on dialysis. Can you share any thoughts on this subgroup of patients and how their results compared with the rest of the study group? And compared with men with renal disease? In my experience, these vessels are smaller, calcified especially in women and tend to fair worse both at surgery and with endovascular treatment.
(2) For planning purposes, did you use CT angiograms or MRAs routinely for planning of the case prior to treatment?
(3) Do you have any data describing the balloon and stent diameters used in women compared with men correlating that with body size and weight? I think it would be interesting to see if women required smaller or similar size endovascular interventions and still had comparable results.
(4) With the increasing use and understanding of crossing devices, the surgeons in this study did not use them even though most of the vessels intervened were the SFA. Why? Were there any characteristics or selection of these patients that limited the use of crossing devices? If yes, what were they?
(5) Could you provide us some data in how you handle your endovascular failures? Do you always reintervene? Do you go straight to surgery? What are your results with failures?

Finally, and probably the most important question, we must now start thinking beyond just doing these procedures technically and reporting our results. Can you speculate how to design the next important studies and what are the important aspects of those studies for vascular specialists to help treat our patients?

I thank you for the opportunity to discuss your very well written paper and eagerly look forward to your responses. Thank you.

Dr DeRubertis. Dr. Singh, thank you for your discussion and your very insightful comments.

First, I would like to a comment on the question of whether our results are generalizable to the entire population. As vascular surgeons continue to become increasingly familiar with different devices and gain advanced endovascular expertise, I think these results will be obtainable across the board in both community and academic centers. I think the prerequisite, however, is a true commitment to undertaking these types of procedures, including the more complex ones. Part of this commitment involves securing access to the types of imaging systems required and becoming familiar with the breadth of devices required for the more difficult cases.

In response to your question regarding patients with chronic renal insufficiency, in this series approximately 30% of patients had an elevated creatinine consistent with chronic renal disease. When looking at all interventions, the overall rate of worsening renal dysfunction was just over 2%, and this was equivalent between men and women. In patients with a baseline creatinine less than 3, the rate of worsening renal dysfunction was around 13% and the need for hemodialysis was 0.3%. In patients with a creatinine greater than 3, these rates were about 40% and 25%, respectively, and only two of the four patients who required dialysis went on to become chronically dialysis dependent. Both of these patients had baseline creatinine of greater than 4 and were therefore already moving

toward dialysis dependence. All four patients who required dialysis were intervened upon for limb-threat and had no available conduit.

In terms of the outcomes between men and women, there was no overall difference between genders in terms of patency and limb salvage, nor were there any differences between men and women when stratified by baseline preoperative creatinine level. Furthermore, while other studies have demonstrated differential outcomes in patients with end-stage renal disease on hemodialysis, we did not observe such a difference. So to summarize our experience with patients with chronic renal insufficiency, we believe percutaneous interventions can be done safely provided the baseline creatinine is under the 2.5 to 3 range and provided one is conscious of the contrast usage. The vast majority of interventions can be performed using small volumes of 50% contrast by performing selective runs on appropriate imaging equipment and avoiding unnecessary contrast exposure.

In terms of vessel diameters between men and women, we did not see a difference in balloon and stent sizes between genders. In the SFA, the average diameter stent was 5.9 for women and 6.1 for men, which was statistically equivalent. The differences in stent sizes were based on location, SFA vs popliteal/tibial.

When determining the point at which your endovascular approach has failed and the time to perform a surgical bypass has come, some of the issues to keep in mind include the patient's conduit, their overall medical condition or surgical risk, and the goals of treatment. In a 50-year-old claudicant who has adequate autologous conduit, one might try a percutaneous intervention one time and when that fails 6 or 8 months later that patient may well want the most durable solution to his problem and may elect at that time for a surgical bypass. On the other hand, in a 90-year-old patient with recent MI who presents with a nonhealing toe ulcer, two or three percutaneous interventions, if necessary, may be appropriate in order to maintain patency long enough to allow the patient to heal his ulcer and avoid a major operation. I think it largely depends on what the goals of treatment are. While we hold no set limits as far as how many interventions one can undergo, we believe it is of utmost importance to remain conscious of your surgical bypass targets and avoid any maneuvers that risk injury to these vessels.

In terms of the next important studies, one relates to the issue of multiple interventions. We have not yet looked at any cost analysis aspect of these interventions. I suspect that endovascular therapy may well be a reasonably sound approach from a financial standpoint for that first intervention compared with a bypass, especially considering the economic costs of perioperative complications associated with each approach. However, as multiple interventions are performed this cost adds up and may ultimately prove to be very expensive. Like most available studies on these emerging technologies, ours is a retrospective analysis of a prospective database and this methodology brings with it certain biases. All of these modalities need to be further assessed in a prospective randomized fashion in the future.