Impact of metabolic syndrome on the outcomes of superficial femoral artery interventions

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Background: **Metabolic syndrome (MetSyn) is an epidemic in the United States and is associated with early onset of atherosclerosis, increased thrombotic events, and increased complications after cardiovascular intervention. MetSyn is found in ~50% of patients with peripheral vascular disease. However, its impact on peripheral interventions is unknown. The aim of this study is to determine the outcomes of superficial femoral artery (SFA) interventions in patients with and without MetSyn.**

Methods: **A database of patients undergoing endovascular treatment of SFA disease between 1999 and 2009 was retrospectively queried. MetSyn was defined as the presence of ≥3 of the following criteria: blood pressure ≥130 mm Hg/≥85 mm Hg; triglycerides ≥150 mg/dL; high-density lipoprotein ≤50 mg/dL for women and ≤40 mg/dL for men; fasting blood glucose ≥110 mg/dL; or body mass index ≥30 kg/m^2. Kaplan-Meier survival analyses were performed to assess time-dependent outcomes. Factor analyses were performed using a Cox proportional hazard model for time-dependent variables.**

Results: **A total of 1018 limbs in 738 patients (64% male, average age 67 years) underwent endovascular treatment for symptomatic SFA disease with 45% of patients meeting the criteria for MetSyn. MetSyn patients were more likely to be female ($P = .001$), to present with critical ischemia (rest pain/tissue loss: 55% MetSyn vs 45% non-MetSyn; $P = .001$), have poorer ambulatory status ($P = .001$), and have more advanced SFA lesions (TransAtlantic Inter-Society Consensus II C/D: 51% vs 11%; $P = .001$) and worse tibial runoff ($P = .001$). MetSyn patients required more complex interventions ($P = .0001$). There was no difference in mortality and major adverse cardiac events, but systemic complications (4% vs 1%; $P = .001$) and major adverse limb events (12% vs 7%; $P = .0009$) were significantly higher in the MetSyn group. Immediate postprocedural hemodynamic improvement, resolved or improved symptoms, and restoration of impaired ambulation were equivalent in both groups. Early failure (<6 months) was more common in those with MetSyn. At 5 years, primary, assisted primary, and secondary patencies were not affected by the presence of MetSyn. The presence of MetSyn was associated with a decrease in clinical efficacy, decreased freedom from recurrent symptoms, and decreased freedom from major amputation at 5 years.**

Conclusions: **MetSyn is present in nearly half of the patients presenting with SFA disease. These patients present with more advanced disease and have poorer symptomatic and functional outcomes compared with those patients without MetSyn. (J Vasc Surg 2012;55:985-93.)**

There has been a substantial increase in the prevalence of the prediabetic state, metabolic syndrome (MetSyn), and diabetes mellitus (DM) in the last decade.[1] Projections suggest that these patterns of disease will increase substantially in the next two decades. Coupled to the increase in diabetic conditions is a marked increase in and shift towards endoluminal therapy for superficial femoral artery (SFA) occlusive disease.[2,3] The technology and technical skills in practice have improved and permitted increasingly more challenging lesions to be tackled.[4,5] Multiple reports have demonstrated that presenting symptoms, diabetes, and tibial runoff will affect the anatomic and functional outcomes after SFA intervention.[6-10] We have previously demonstrated that MetSyn has a negative influence on outcomes after carotid intervention and renal intervention.[11,12] The interaction of MetSyn and SFA interventions is unknown. The aim of this study is to examine the impact of MetSyn on endoluminal interventions for SFA disease.

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METHODS

Study design. A database of patients undergoing endovascular treatment of SFA disease between 1999 and 2009 was retrospectively queried. Two groups were identified, those with and without MetSyn. MetSyn was defined as the presence of ≥3 of the following criteria: blood pressure ≥130 mm Hg/≥85 mm Hg; triglycerides ≥150 mg/dL; high-density lipoprotein (HDL) ≤50 mg/dL for women and ≤40 mg/dL for men; fasting blood glucose ≥110 mg/dL; or body mass index (BMI) ≥30 kg/m^2.[13] We substituted a BMI score ≥30.0 as a positive score

instead of an abdominal circumference >102 cm or >88 cm for male or female patients, respectively. Data utilization fell under the category of secondary use of pre-existing data as defined by the Institutional Review Board and the Health Insurance Portability and Accountability Act (HIPAA).

Study setting. The setting was an academic medical center with 1000 beds in a catchment area of 5 million people. It is a tertiary and quaternary referral facility.

Methodology. For each patient captured, demographics, symptoms, existing comorbid conditions, and risk factors for atherosclerosis were identified. Risk factors were identified for each patient and corrected through their primary care providers (see Appendix, online only). Therapy for individual patients was dictated by individual attending physician preference and was not regulated by unit guidelines. All patients received aspirin daily (81 mg or 325 mg) as a general cardiovascular protection agent.

Noninvasive studies were performed initially on all patients receiving a work-up for peripheral arterial disease. Patients with serious symptoms or signs of severe stenosis/occlusion based upon the initial noninvasive tests received angiograms. Angiograms and angiographic reports were reviewed; lesions were described by length, calcification, and patency and then categorized under the TransAtlantic Inter-Society Consensus (TASC)-II system.[14] The preoperative distal runoff was scored by the number of patent tibial vessels and according to a modification of SVS criteria employed for determining bypass runoff (using the cumulative score for the distal popliteal from knee joint to first tibial branch; maximum, 9 + 1) and each of the tibial vessels (maximum, 3 each) giving a maximum possible total score of 19.[9]

Patients were on aspirin preoperatively and in the last 5 years patients also received clopidogrel preoperatively. Angioplasty was performed with a patient under systemic heparin administration (40-60 units/kg), and completion angiography was performed to assess the technical result. Stents were utilized (at the discretion of the operator) primarily or as an adjunct for flow-limiting dissections, intimal flaps, or poor technical results (≥50% residual stenosis). No covered stents were used. No procedures or interventions were performed that could have potentially jeopardized the outflow vessel for a bypass. The complexity of each intervention was scored according to the ad hoc system described by DeRubertis et al[6] in which 1 point was awarded for an intervention in the iliac, femoral, or tibial segments of the leg.

Patients who had a successful endoluminal intervention received 75 mg of clopidogrel daily. While a patient was on clopidogrel, aspirin therapy was maintained at 81 mg per day. Patients on clopidogrel prior to the intervention remained on clopidogrel after the intervention. Clopidogrel therapy was continued for 30 days after the intervention. Patients underwent routine duplex ultrasound follow-up at 1, 3, and every 6 months following their procedure using criteria previously described.[7] During follow-up, angiography was only performed if noninvasive studies suggested restenosis/occlusion (positive duplex scan with a drop in ankle-brachial index [ABI] of >0.15 and toe-brachial index [TBI] of >0.1), and the patient had recurrent symptoms.

Table I. Characteristics of patients

	No MetSyn	*MetSyn*	P *value*
Demographics			
Patients	408	330	—
Limbs treated	544	474	—
% male	70	57	.001
Average age (mean ± SD, years)	67 ± 15	67 ± 13	.99
Symptoms			
Claudication	63%	45%	
Rest pain/tissue loss	37%	55%	.001
Comorbidities			
Modified cardiac risk index	2.8 ± 1.6	3.3 ± 1.7	.001
Smoking history	76%	75%	.76
Current smoker	19%	19%	1
Coronary artery disease	35%	43%	.01
Hypertension	84%	98%	.001
Diabetes	38%	72%	.001
Hyperlipidemia	55%	79%	.001
Statin	50%	72%	.001
Cerebrovascular disease	23%	23%	1
Chronic kidney disease	13%	21%	.001
Hemodialysis	5%	14%	.001
Hypothyroidism	9%	13%	.04
Hypercoagulability	8%	4%	.009
Preoperative living status			
Independent	63%	45%	.001
Dependent	37%	55%	
Preoperative ambulatory status			
Ambulatory	55%	37%	.001
Ambulatory/homebound	35%	34%	
Nonambulatory/transfer	11%	28%	
Nonambulatory/bedridden	0%	1%	

MetSyn, Metabolic syndrome.

Statistical analysis. All statistical analyses were performed on an "intention-to-treat" basis. Measured values are reported as percentages or means ± SD. Patency and limb salvage rates were calculated using Kaplan-Meier analyses and reported using current SVS criteria and objective performance goals.[15,16] Cox regression was performed for independent variables. Standard errors are reported in Kaplan-Meier analyses. Definitions of all outcome parameters used are shown in the appendix. Analyses were performed using JMP software version 7.0 (SAS Institute, Cary, NC).

RESULTS

Patient population. A total of 1018 limbs in 738 patients underwent endovascular treatment for symptomatic SFA disease and 45% of patients matched the criteria for MetSyn. In the non-MetSyn group, 70% were male, while in the MetSyn group, 57% were male (Table I); 63% of the interventions were for lifestyle-limiting claudication in the non-MetSyn group, while 45% were performed for this reason in those patients with MetSyn. Age was equivalent in

both groups (Table I). Past smoking history and current smoking were equal between the groups (Table I). There were a significantly higher number of patients with coronary artery disease and a greater modified cardiac risk index in the MetSyn patients compared with the non-MetSyn patients (Table I). Hypertension, hyperlipidemia, diabetes, chronic renal disease, and hypothyroidism were more prevalent in those with MetSyn (Table I). There was a twofold increase in the number of patients on hemodialysis in MetSyn. Approximately 50% of patients in the non-MetSyn cohort and 72% in the MetSyn cohort were on statins (Table I). In MetSyn, there were a higher number of patients considered dependent and a greater number with a reduced or nonambulatory status (Table I). Patients presenting with MetSyn had a greater number of TASC-II C and D lesions (51% vs 31%; $P = .001$). When traditional runoff scores were used to grade the runoff, there was no difference in the group averages between non-MetSyn and MetSyn (number of tibial vessels, 2.02 ± 0.82% vs 1.92 ± 0.83%, non-MetSyn vs MetSyn; $P = .055$); however, when a modified SVS runoff score was used, the runoff in the MetSyn group was significantly worse (modified SVS runoff score, 6.6 ± 4.6% vs 7.0 ± 4.5%, non-MetSyn vs MetSyn; $P = .001$).

Immediate outcomes. The technical failure rates were 3% and 4% for non-MetSyn and MetSyn, respectively. However, no patient in either group required emergent conversion to open surgery. Eventual need for open bypass surgery is described below (Fig 1, *D* and *E*). Approximately a third of patients in each group required recannulization for occlusion (Table II). The majority of cases were treated by angioplasty; however, the use of primary stenting was twofold higher in the MetSyn group, which may reflect the aforementioned differences in TASC-II lesion categories. Overall stent usage was significantly higher in the MetSyn group (Table II). Patients with MetSyn had a higher level of complexity in their cases than the non-MetSyn cases (Table II). An equal number of inflow procedures in the aortoiliac segment were performed, whereas there were significantly more tibial interventions in the MetSyn group, correlating with the previously mentioned poorer runoff scores. Mortality was equivalent in both groups, despite the increased burden of coronary disease in the MetSyn group (Table I). Total morbidity was similar between the two groups, but there was an increase in the incidence of systemic complications in the MetSyn group (Table III). Thirty-day major adverse cardiac events (MACE) were equivalent but 30-day major adverse limb events (MALE) were higher in the MetSyn group compared with the non-MetSyn group (Table III).

Hemodynamically, there was a marked increase in ABIs in both groups, with more than 80% of patients having a rise in their ABI of >0.15. There was no difference between non-MetSyn and MetSyn groups (Table IV). Following intervention in non-MetSyn and MetSyn groups, 83% and 87% of patients were considered to have improved or resolved symptoms, respectively (Table IV). There was a significant improvement in ambulatory status in both groups after intervention and both groups had equivalent responses (Table IV). There was no difference in discharge status between the groups (Table IV).

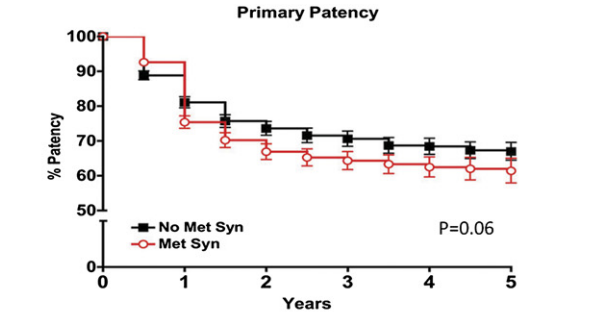
Long-term anatomic outcomes. There was no significant difference in the primary (67% ± 3% vs 61 ± 4%, non-MetSyn vs MetSyn; $P = .06$), assisted primary (77% ± 2% vs 73% ± 4%; $P = .19$), or secondary patency (78% ± 2% vs 77 ± 3%; $P = .27$) of the non-MetSyn and MetSyn groups at 5 years (Fig 1, *A-C*). There was a significant association ($P = .03$) with early failure (<6 months) in the MetSyn group (61%) compared with the non-MetSyn group (47%). Target vessel revascularization (TVR, 81% ± 2% vs 79% ± 3%, non-MetSyn vs MetSyn; $P = .14$) and target extremity revascularization (TER), 79% ± 2% vs 77 ± 3%, non-MetSyn vs MetSyn; $P = .10$) were equivalent at 5 years (Fig 1, *D* and *E*).

Long-term functional outcomes. Overall mortality was higher in the MetSyn group, with patient survival rates of 71% ± 2% and 53% ± 3% at 5 years in the non-MetSyn and MetSyn groups, respectively (Fig 2, *A*). Amputation-free survival was significantly worse in the MetSyn group (Fig 2, *B*). Freedom from recurrent symptoms was superior in the non-MetSyn group (Fig 2, *D*). The 5-year rate of freedom from recurrent symptoms was 62% ± 2% and 51% ± 6% in the non-MetSyn and MetSyn groups, respectively ($P = .03$). Limb salvage was significantly better in the non-MetSyn group compared with the MetSyn group (Fig 2, *C*). The 5-year limb salvage rate was 90% ± 2% and 84% ± 3% in the non-MetSyn and MetSyn groups, respectively. Three percent and 8% of patients presenting with claudication in the non-MetSyn and MetSyn groups, respectively, suffered a major amputation ($P = .23$), while 27% and 48% presenting with critical limb ischemia in the non-MetSyn and MetSyn groups suffered a major amputation ($P = .02$). Clinical success defined as freedom from recurrent symptoms, maintenance of ambulation, and absence of a major amputation was significantly higher (60% ± 3% and 39% ± 5% at 5 years) in the non-MetSyn group compared with the MetSyn group (Fig 2, *E*).

A Cox regression subanalysis was performed on both MetSyn and non-MetSyn groups for complexity score/multilevel intervention as well as patient factors creatinine > 2, hemodialysis, and TASC C/D. Each was censored by the following: primary patency, assisted primary patency, secondary patency, survival, freedom from recurrent symptoms, and clinical efficacy. Complexity score/multilevel intervention was an independent risk factor in freedom from recurrent symptoms ($P = .01$) and clinical efficacy ($P = .003$). Creatinine > 2 was an independent risk factor in status of limb/toe amputation or greater freedom from amputation and amputation-free survival ($P = .02$).

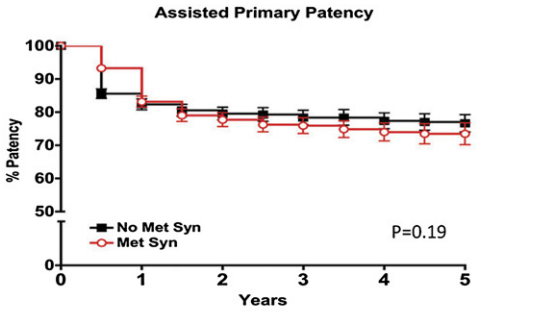
DISCUSSION

Summary. In this study, we analyzed the presence of MetSyn and its relationship to short- and long-term outcomes in 738 patients undergoing SFA interventions for symptomatic lower extremity arterial disease. We found that MetSyn patients were more likely to be female, to



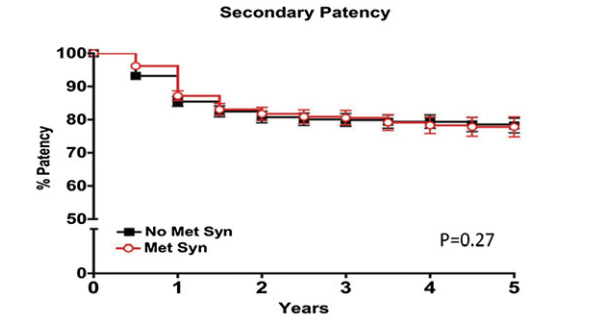
Year	0	1	2	3	4	5
No Metabolic Syndrome	545	417	336	295	254	208
Metabolic syndrome	474	332	252	200	139	97

A



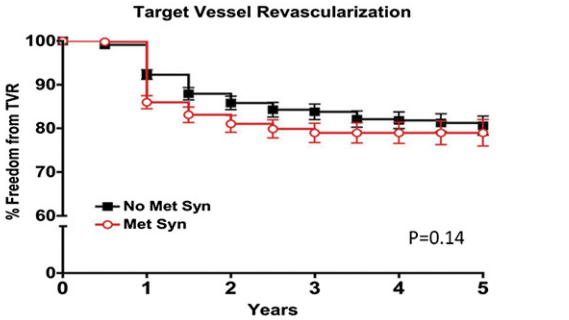
Year	0	1	2	3	4	5
No Metabolic Syndrome	545	434	365	327	286	237
Metabolic syndrome	474	363	281	222	154	109

B



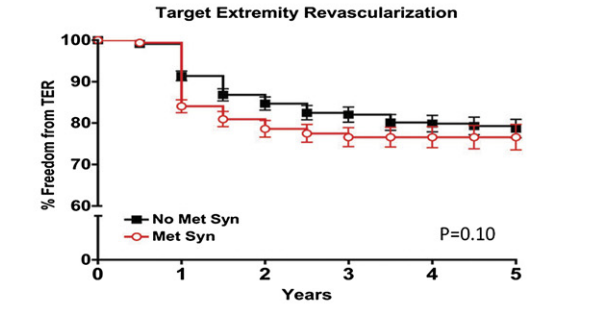
Year	0	1	2	3	4	5
No Metabolic Syndrome	545	439	371	332	293	241
Metabolic syndrome	474	380	297	239	170	125

C



Year	0	1	2	3	4	5
No Metabolic Syndrome	545	474	397	353	298	248
Metabolic syndrome	474	374	299	245	179	122

D



Year	0	1	2	3	4	5
No Metabolic Syndrome	545	471	393	349	293	243
Metabolic syndrome	474	367	293	240	174	122

E

Fig 1. Anatomic outcomes: Life table analysis of patients with and without metabolic syndrome. Data are the mean ± standard error of the mean and number of limbs at risk shown in the table. No *error bars* are shown if the standard error of the mean is >10%, and the data set terminates if the number at risk is <10. **A,** Primary patency; **B,** assisted primary patency; **C,** secondary patency; **D,** target vessel revascularization; and **E,** target extremity revascularization.

present with critical ischemia (rest pain/tissue loss), have poorer ambulatory status, have more advanced SFA lesions, and have worse tibial runoff ($P = .001$). Patients with MetSyn required more complex interventions ($P = .0001$). There was no difference in mortality and MACE, but systemic complications (4% vs 1%; $P = .001$) and MALE (12% vs 7%; $P = .0009$) were significantly higher in the MetSyn group. Immediate postprocedural hemodynamic/

Table II. Procedures and complexity

	No MetSyn	*MetSyn*	P *value*
Intervention			
Recannulization	36%	33%	.32
Angioplasty	67%	58%	.008
Primary stenting	15%	24%	
Laser and directional atherectomy	3%	5%	
Stent usage	31%	43%	.002
Adjunctive interventions			
Aortoiliac intervention	9%	9%	1.0
Tibial intervention	7%	18%	.001
Complexity score	1.21 ± 0.44	1.37 ± 0.57	.0001

MetSyn, Metabolic syndrome.

Table III. Mortality, morbidity, and objective performance goals

	No MetSyn	*MetSyn*	P *value*
Mortality and morbidity			
Mortality	2.8%	1.7%	.29
Morbidity	15%	15%	1
Systemic	1%	4%	.001
Local	6%	4%	.16
Lesion	13%	14%	.65
Objective performance goals			
30-day MACE	2.9%	2.1%	.55
30-day MALE	7%	12%	.009

MACE, Major adverse cardiac events; *MALE*, major adverse limb events; *MetSyn*, metabolic syndrome.

Table IV. Hemodynamic changes and immediate symptom relief

	No MetSyn	*MetSyn*	P *value*
Hemodynamic changes			
Change in ABI	0.25 ± 0.32	0.28 ± 0.33	.14
% ABI increase >0.15	80%	82%	.42
Immediate symptom relief			
Resolved	48%	42%	.002
Improved	35%	45%	
No change	16%	11%	
Deterioration	1%	2%	
Postoperative ambulatory status			
Ambulatory	86%	81%	.26
Ambulatory/homebound	7%	9%	
Nonambulatory/transfer	7%	9%	
Nonambulatory/bedridden	0%	1%	
Discharge status			
Home	75%	76%	.70
Rehabilitation facility	17%	15%	
Skilled nursing facility	7%	8%	
Hospital	1%	1%	

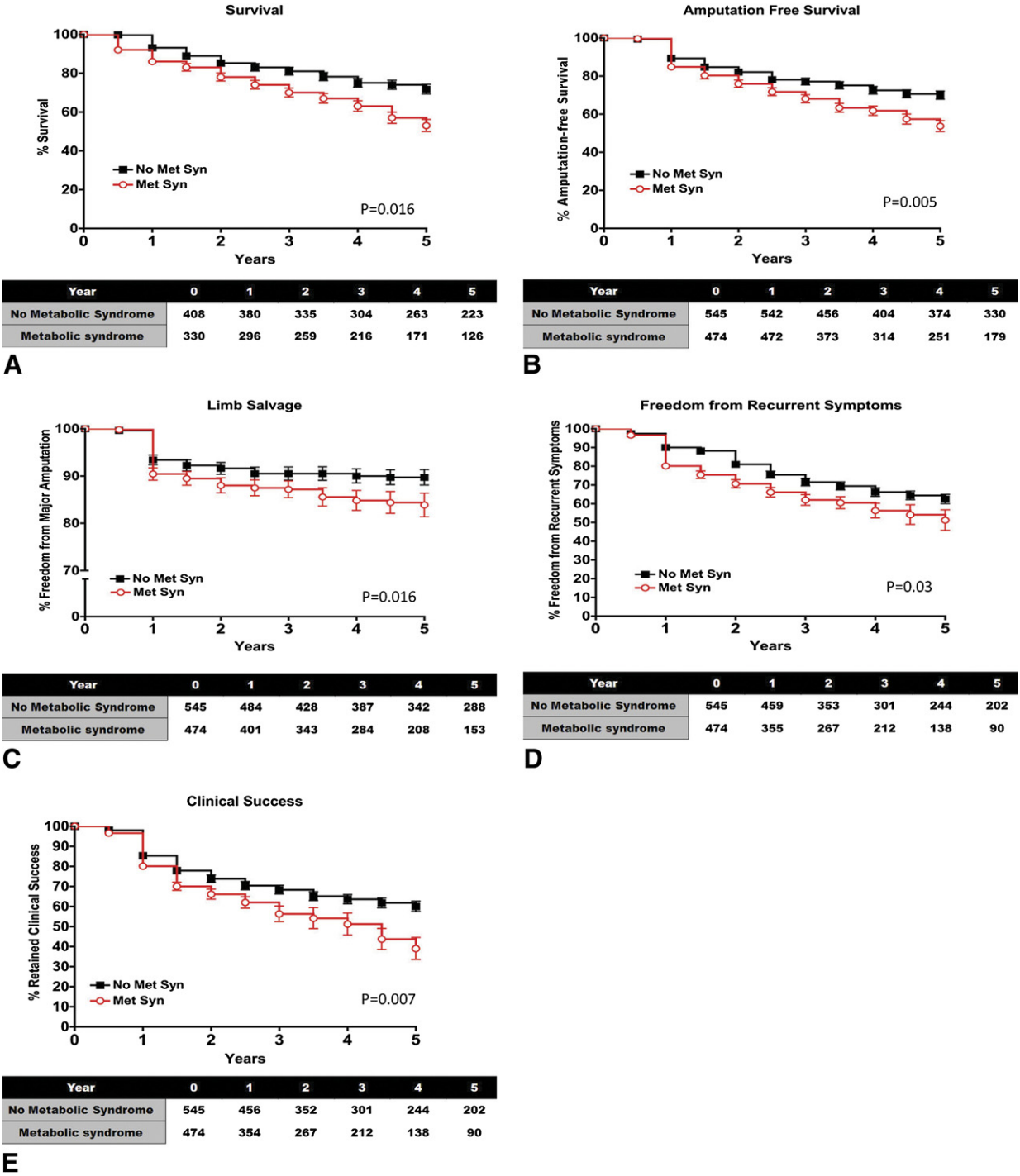
ABI, Ankle-brachial index; *MetSyn*, metabolic syndrome.

symptom improvement and restoration of impaired ambulation were equivalent in both groups. Early failure (<6 months) was more common in those with MetSyn. At 5 years, primary, assisted primary, and secondary patencies were not affected by the presence of MetSyn. This may indicate the most likely time frame that MetSyn intervention will fail anatomically, within 6 months, though there is no significant difference between the groups at 5 years in regards to arterial patency to the ankle. The presence of MetSyn was associated with lower survival, a decrease in clinical efficacy, reduced freedom from recurrent symptoms, and diminished freedom from major amputation at 5 years.

Patients. MetSyn was found in 45% of patients presenting with symptomatic SFA disease. A survey of patients with intermittent claudication and ABI < 0.90 showed that 53% met the revised version of the Adults Treatment Panel III (rATP III) criteria for MetSyn.[17] In women, MetSyn is associated with an increased risk of future symptomatic peripheral arterial disease. The prevalence of MetSyn in the general adult population in developing countries has been estimated to be between 22% and 39% and varies depending on the definition used and on ethnicity.[18-20] Using either World Health Organization (WHO) or National Cholesterol Education Program (NCEP) definitions, MetSyn is associated with future coronary heart disease events and type 2 diabetes. Both definitions will predict cardiovascular mortality, while the NCEP definition can predict all-cause mortality. People with MetSyn and a Framingham risk score >20% have an increased risk of major coronary events over the next 10 years compared with people without MetSyn and the same risk score.[21] Well-established indicators of the increased cardiovascular risk, such as low ABI and increased C-reactive protein (CRP) levels, also cluster with MetSyn.[22] We found that the overall mortality was significantly much higher in the MetSyn group than in the non-MetSyn group. The patients that had a higher baseline modified cardiac risk index and the morbidities associated with cardiovascular mortality were clustered in the MetSyn group. These included the diseases associated with MetSyn (hypertension, hyperlipidemia, and diabetes) and those not associated with MetSyn (chronic renal insufficiency, hemodialysis dependency, and hypothyroidism). This clustering of comorbidities was associated with a lower level of independence and mobility. Many of these findings are associated with presence of obesity.

Metabolic syndrome. Identification of MetSyn allows clinicians to move away from a strategy based on management of a single risk factor to one that focuses on a constellation of synergistic risk factors.[23] There are, however, multiple definitions of MetSyn.[13,24] Our definition is similar to the NCEP definition in the scoring system for four of the five criteria.[25] We substituted abdominal obesity with a BMI >30 kg/m^2. Due to the retrospective design of our study, we did not have abdominal circumference data for the patients in the study groups. The WHO definition of MetSyn permits substituting an elevated BMI for abdominal obesity.

Presentation. In this study, we found that the patients with MetSyn presented with more advanced symptoms of rest pain and tissue loss than those without MetSyn; the more significant symptoms were reflected in more ad-



Year	0	1	2	3	4	5
No Metabolic Syndrome	408	380	335	304	263	223
Metabolic syndrome	330	296	259	216	171	126

A

Year	0	1	2	3	4	5
No Metabolic Syndrome	545	542	456	404	374	330
Metabolic syndrome	474	472	373	314	251	179

B

Year	0	1	2	3	4	5
No Metabolic Syndrome	545	484	428	387	342	288
Metabolic syndrome	474	401	343	284	208	153

C

Year	0	1	2	3	4	5
No Metabolic Syndrome	545	459	353	301	244	202
Metabolic syndrome	474	355	267	212	138	90

D

Year	0	1	2	3	4	5
No Metabolic Syndrome	545	456	352	301	244	202
Metabolic syndrome	474	354	267	212	138	90

E

Fig 2. Functional outcomes: Life table analysis of patients with and without metabolic syndrome. Data are the mean ± standard error of the mean and number of patients or limbs at risk shown in the table. No *error bars* are shown if the standard error of the mean is >10% and the data set terminates if the number at risk is <10. **A,** Survival; **B,** amputation-free survival; **C,** limb salvage; **D,** freedom from recurrent symptoms; and **E,** clinical success.

vanced anatomic disease (greater number of TASC C and D lesions) and a poorer tibial runoff. Maksimovic et al[26] have shown that the degree of peripheral arterial disease clinical manifestations is not related to gross MetSyn score, a finding we also noted in this study. However, gangrene was significantly positively associated with increased fasting glucose, high-sensitivity CRP (hsCRP), and lower education levels.[26] We have shown that the presence of diabetes and

chronic renal insufficiency will affect the outcomes after SFA intervention.[7,8] Several other authors have demonstrated that the severity of presenting symptoms,[27,28] lesion severity,[28,29] and the poor runoff will affect the outcomes of SFA interventions.[9,29]

Anatomic outcomes. The presence of MetSyn did not influence the overall technical success of the procedures, but the procedures were more frequently multilevel and required a higher number of recanalizations and stent placements. This reflects the presence of the more advanced disease. MetSyn patients were more likely to fail early, within the first 6 months, which has been shown to be a poor predictor of the success of further interventions in the SFA.[30,31] Anatomically, this is similar to studies of interventions in other vessels, namely the renal and coronary arteries,[12,32,33] where the presence of MetSyn did not influence the anatomic outcomes. Overall mortality and morbidity was equivalent after intervention between the groups, with the exception that the MetSyn group experienced more systemic complications. Thirty-day MACE was equivalent but 30-day MALE was high in the MetSyn group compared with the non-MetSyn group; this was not driven by major amputations at 30 days, as this was equivalent between the groups. Similar findings have been seen in the coronary and renal literature.[12,34]

Functional outcomes. Functional outcomes, namely reduction in symptoms, preservation of limb, and maintenance of ambulation must remain the ultimate goal of all vascular interventions, including those in the SFA. There has been a decrease in major amputations reported in the Nationwide Inpatient Sample (NIS) associated with an increase in endoluminal interventions and a decrease in surgical procedures over the past few decades for a variety of reasons.[35] The most significant finding in this study is that the presence of MetSyn portends a worse functional outcome for SFA interventions. The presence of obesity and MetSyn significantly increased the risks of subsequent cardiac events among patients who underwent percutaneous coronary intervention.[36-40] Similar poor functional outcomes have been seen after renal interventions in patients with MetSyn.[12] Patients with MetSyn had an overall poorer clinical efficacy (freedom from recurrent symptoms, maintenance of ambulation, and absence of a major amputation) than those without MetSyn. This was despite the fact that there were an equivalent number of patients showing an ABI rise >0.15 combined with the majority of the patients showing initial improvement or resolution of symptoms, respectively. These changes in symptoms were coupled with a significant improvement in ambulatory status in both groups. Long-term mortality was higher and amputation-free survival was significantly worse in the MetSyn group. Notably this lower amputation-free survival was also true for MetSyn patients with claudication only and no rest pain/tissue loss. This not only reinforces the authors' practice of reserving interventions in claudicants for those with subjectively severe and disabling claudication that limits the patient's activity such that it is exacerbating existing comorbidities. It also adds further caution in proceeding with intervention in claudicants with MetSyn going forward. This reflects the higher modified cardiac risk index and cluster of comorbidities and the greater number of patients presenting with critical limb ischemia and advanced anatomic disease. It must also reflect the presence of diabetes and hemodialysis conditions in the MetSyn patients. While the immediate improvements in presenting symptoms were gratifying, the freedom from recurrent symptoms and limb salvage were worse, with 27% of non-MetSyn patients and 48% of MetSyn patients presenting with critical limb ischemia suffering a major amputation during follow-up.

Study limitations. This study is retrospective in nature and the clinical decision making was individualized, not driven by a standard protocol. The definitions of MetSyn are continually changing, and we have used a surrogate marker of body adiposity (BMI calculation from admission height and weight) that is not currently utilized in all definitions of MetSyn. We cannot discount completely the influence of diabetes, obesity, and end-stage renal disease on the results, but it appears that patients with MetSyn effectively cluster the worst comorbidities to them at presentation.

CONCLUSIONS

Patients with MetSyn present with more advanced symptoms, more complex atherosclerotic disease, and require more complex interventions. While anatomic outcomes are not influenced by MetSyn, functional outcomes (reduction in symptoms, preservation of limb, and maintenance of ambulation) are worse and long-term survival is shorter. MetSyn should be considered a risk factor for poor outcomes during SFA interventions.

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AUTHOR CONTRIBUTIONS

Conception and design: CS, MD
Analysis and interpretation: CS, MD
Data collection: CS, JA, JB, HE, EP, JN, MD
Writing the article: CS
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DISCUSSION

Dr Scott Stevens (*Knoxville, Tenn*). This presentation from Smolock, Lumsden, Davies and Team Vascular at The Methodist/DeBakey Heart & Vascular Center in Houston addresses the important topic of outcomes for SFA interventions in patients with metabolic syndrome. They studied 1014 SFA interventions over a 10-year period and found that nearly half of these were in patients with metabolic syndrome. Their study showed that in this subset, patients with metabolic syndrome were more likely to be female, have more advanced lesions, and present with critical limb ischemia. The study also demonstrated higher morbidity and decreased clinical efficacy, as manifest by recurrent symptoms, decreased patency, and more amputations. Of note, periprocedural mortality was not increased in patients with metabolic syndrome. This study is important because it addresses outcomes in the arena of lower extremity interventions and in the era of comparative effectiveness, it is going to be all about outcomes. Despite the huge increase of SFA interventions and the wide array of therapeutic options available, we still have no evidence-based data to guide us. It is pivotal that, as vascular surgeons, we step up and participate in registries, trials, and critical outcomes analysis to continue our leadership position and bring the best treatment for our patients.

I would like to congratulate Dr Smolock and the vascular team at The Methodist/DeBakey Heart & Vascular Center in Houston for an excellent and timely paper.

Chris, I have four questions:

1. Your data showed higher periprocedural morbidity and worse long-term outcomes, but not worse periprocedural mortality in the patients with metabolic syndrome – any ideas why?
2. Do you think metabolic syndrome in this study was a surrogate for anatomic and morphologic predictors of poor outcomes or does it represent a systemic effect?
3. Because of worse outcomes in patients with metabolic syndrome, have you raised the threshold for intervention in this subset?
4. Considering your results, what changes have you made in your practice to reduce vascular risk factors in patients with metabolic syndrome?

Dr Christopher J. Smolock. Thank you, Dr Stevens. For mortality, it was the same between the groups in the periprocedural period. However, mortality was significantly higher for the metabolic syndrome group over the 5-year period. I think the similar and low mortality in the 30-day period reflects the fact that these were local procedures not done under general anesthesia. There are some negative reports regarding patients with metabolic syndrome undergoing coronary procedures as well as general surgery procedures. This is attributed to these patients receiving general anesthesia with a higher likelihood of systemic complications. We did still see a systemic effect in our complication rate in the periprocedural period and that was not due to local complications but rather cardiac, renal, pulmonary, and other systemic types of complications. I also hope that the low periprocedural mortality has to do with our risk reduction strategies preoperatively. This also leads into your last question about what we did differently. We found that our use of statins, β-blockers, and aspirin were not at the levels we would like them to be. Therefore, we have focused on initiating and maintaining these medications when appropriate on all of our patients preoperatively, perioperatively, and upon discharge. In addition, if they meet criteria, we offer referral to a bariatric center. Regarding your second question about small targets, I do not think that the difference with metabolic syndrome is due to poor or small targets. That is based on some of the data we showed related to runoff score. By number of tibial vessels, which has been related to better outcomes, there was no difference between the groups. There was also no difference between groups as measured by SVS runoff score. Diabetes of course is a risk by itself for poor targets or small targets so there may be something there, but not that you could measure anatomically by the aforementioned metrics. And finally, regarding the general approach of the group to intervening for this disease process, we try to be conservative for claudication, unless it is life altering. We are aggressive with an endovascular approach as a first line for critical ischemia.

APPENDIX (online only).

Definitions. Coronary artery disease was defined as a history of angina pectoris, myocardial infarction, congestive heart disease, or prior coronary artery revascularizations. Cerebrovascular disease was defined as a history of stroke, transient ischemic attack, or carotid artery revascularization. Chronic renal impairment was defined as an eGFR <60 mL/min/1.73 m^2 or patient on dialysis. Hypertension was defined as a systolic blood pressure >150 mm Hg or diastolic blood pressure >90 mm Hg on three occasions during a 6-month period. Hypercholesterolemia was defined as fasting serum concentrations of cholesterol >200 mg/dL, a LDL >130 mg/dL, or triglycerides >200 mg/dL. Diabetes was defined as a fasting plasma glucose >110 mg/dL or an HbA1c > 7%. Non-insulin-dependent diabetes mellitus was defined as any patient with diabetes mellitus who did not routinely receive insulin therapy for their diabetes management. Insulin-dependent diabetes mellitus was defined as any patient with diabetes mellitus who routinely received insulin therapy. Modified cardiac risk index was used to classify the preoperative risk of major cardiac events through a point system based on patient history and physical examination as well as the proposed intervention.[41] TASC-II classification of disease severity for femoral lesions was used to define the categories of lesions.[14] A death within 30 days of the procedure was considered procedure related. A major complication was defined as any event, regardless of how minimal, not routinely observed after endoluminal therapy that required treatment with a therapeutic intervention or rehospitalization within 30 days of the procedure. Systemic complications were those related to cardiac, pulmonary, or renal systems as well as sepsis. Local complications were those related to access site, surgical wounds, and the treated limb. MACE was defined as a myocardial infarction, stroke, or death (any cause) within 30 days.[16] Pre- and postprocedural symptoms were defined by SVS criteria[15] and a drop in symptom score of 1 or more in follow-up was considered recurrent symptoms. MALE was defined as an above-ankle amputation of the index limb or major reintervention (new bypass graft, jump/interposition graft revision, or thrombectomy/thrombolysis) within 30 days.[16] Primary, assisted primary, and secondary patency rates were defined in accordance with the reporting standards of the SVS.[15] Freedom from TVR was considered the absence of a percutaneous reintervention or bypass on the initial target vessel or major ipsilateral amputation of the index limb. Freedom from TER was considered the absence of a percutaneous reintervention/bypass on or major ipsilateral amputation of the index limb. Freedom from recurrent symptoms was considered the absence of recurrent ipsilateral symptoms in or need for ipsilateral amputation of the index limb. [9] Limb salvage was considered the freedom from ipsilateral major amputation of the index limb.[15] Amputation-free survival was defined as freedom from above-ankle amputation of the index limb or death. Clinical efficacy was defined as the absence of recurrent symptoms, maintenance of ambulation, and limb preservation in the index limb.