

Preoperative coronary revascularization is it still relevant?

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8th International Conference

Acute Cardiac Care

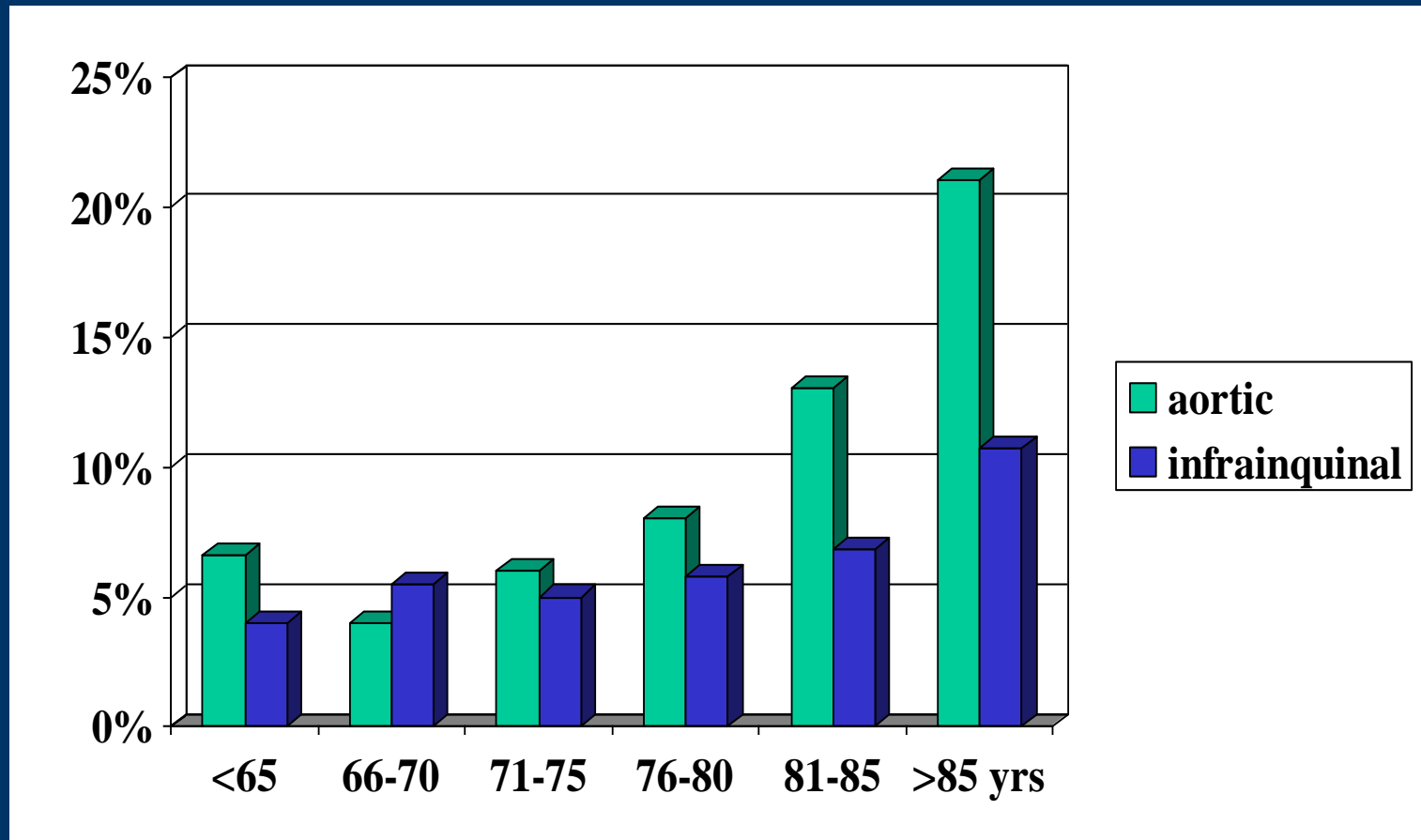
Jerusalem, 18.6.2013

I have no conflict of interest to report
regarding this presentation

Background

- Surgery is associated with stress and hemodynamic instability which might induce myocardial ischemia and injury.
- Cardiac complications constitute the most common cause of postoperative morbidity and mortality.

Immediate implications of peri-operative MI



Perioperative Mortality After Major Vascular Surgery
Fleisher. *Anesth Analg* 1999; 89: 849

Long-term implications of peri-operative MI

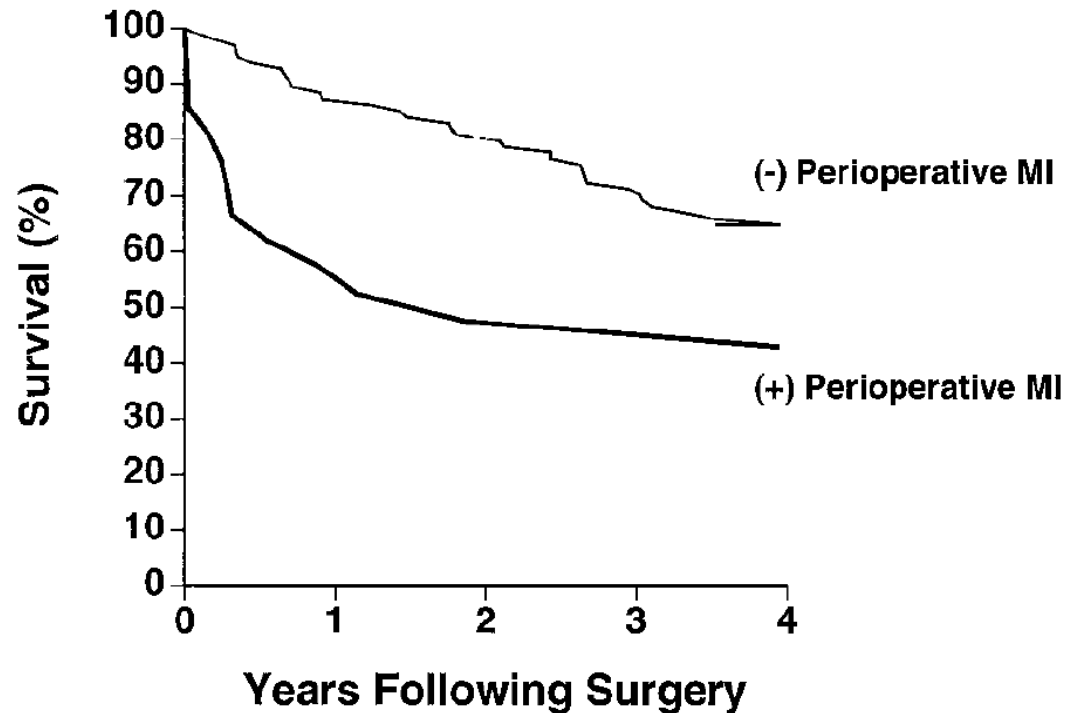


FIGURE 2. Life table analysis shows the long-term survival for 93 patients without and 22 patients with a perioperative MI. Differences in survival curves were statistically significant at 4 years ($p < 0.05$).

The influence of perioperative MI on long-term prognosis following elective vascular surgery.
McFalls et al. Chest 1998

Background

- It is therefore conceivable that candidates for non-cardiac surgery would be studied for cardiac risk factors and coronary artery disease and treated accordingly with preventative measures.

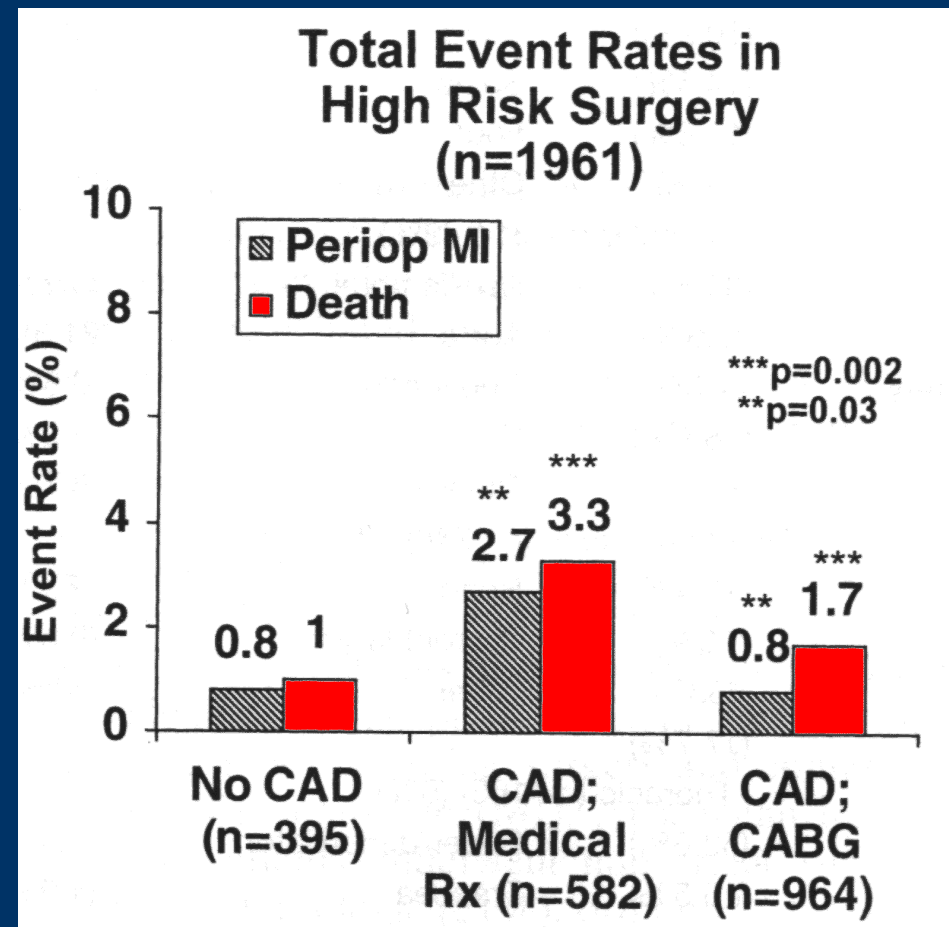
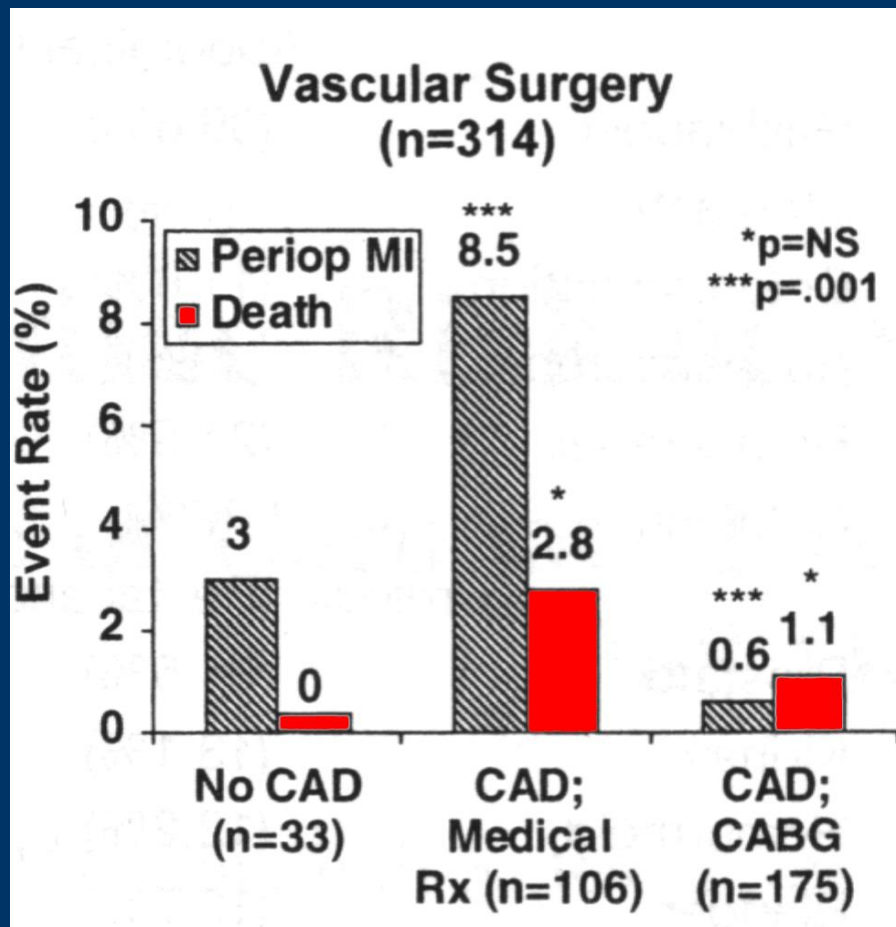
Prevention of peri-operative MI

- Pre-operative stabilization of vulnerable plaques
- Intra- and post-operative management of factors which might increase demand and decrease supply: Pulse, BP, bleeding, stress
- Rapid detection and management of cardiac complications in the postoperative period
- **Pre-operative myocardial revascularization of ischemic regions?**

Scientific reasoning for pre-operative revascularization

Cardiac Risk of Non-Cardiac Surgery

Influence of Coronary Disease and Type of Surgery in 3368 Operations (patients from the **CASS registry**)



Can we diagnose patients at risk?

The Hadassah Vascular Experience

Departments of:
Anesthesiology
Vascular Surgery
Cardiology
Nuclear Medicine

Preoperative thallium scanning (PTS)

During 1990-99 we performed routinely cardiac evaluation with PTS before major vascular surgery

Patients with moderate-severe reversible defects ($> 40\%$ reduction in radioactive counts) were considered for preoperative coronary angiography and possible revascularization by either CABG or PCI

Preoperative Thallium Scanning, Selective Coronary revascularization and Long-Term Survival following Major Vascular Surgery

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(Circulation. 2003;108:177-183.)

Aim

To test whether preoperative thallium scanning and coronary revascularization improve long-term survival following major vascular surgery

Methods

- Retrospective cohort study
- Peri-operative data (clinical, thallium scanning, angiography and revascularization results) and long-term survival were reviewed

502 patients (578 operations)

95 pts
No preop. thallium

407 pts
with preop. thallium

Group I 221 pts
Normal thallium
/ Mild defects

Group II 50 pts
Moderate-severe
Fixed defects

Group III 62 pts
Moderate-severe
Reversible
defects, no
revascularization

Group IV 74 pts
Moderate-severe Reversible
defects, with
revascularization [CABG
(36) / PTCA (38)]

Comparison between groups III and IV

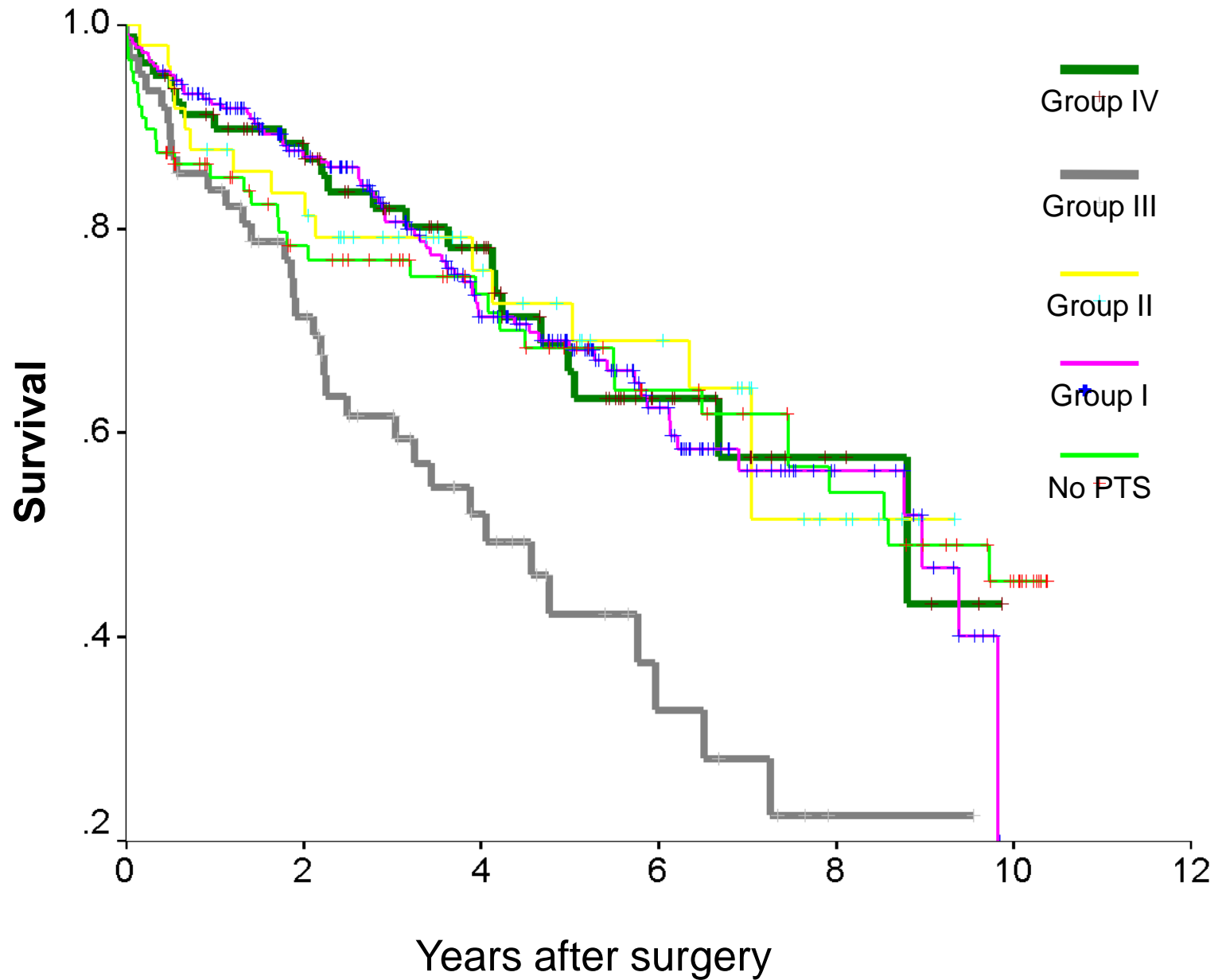
TABLE 2. Preoperative Coronary Angiography and LV Function Results

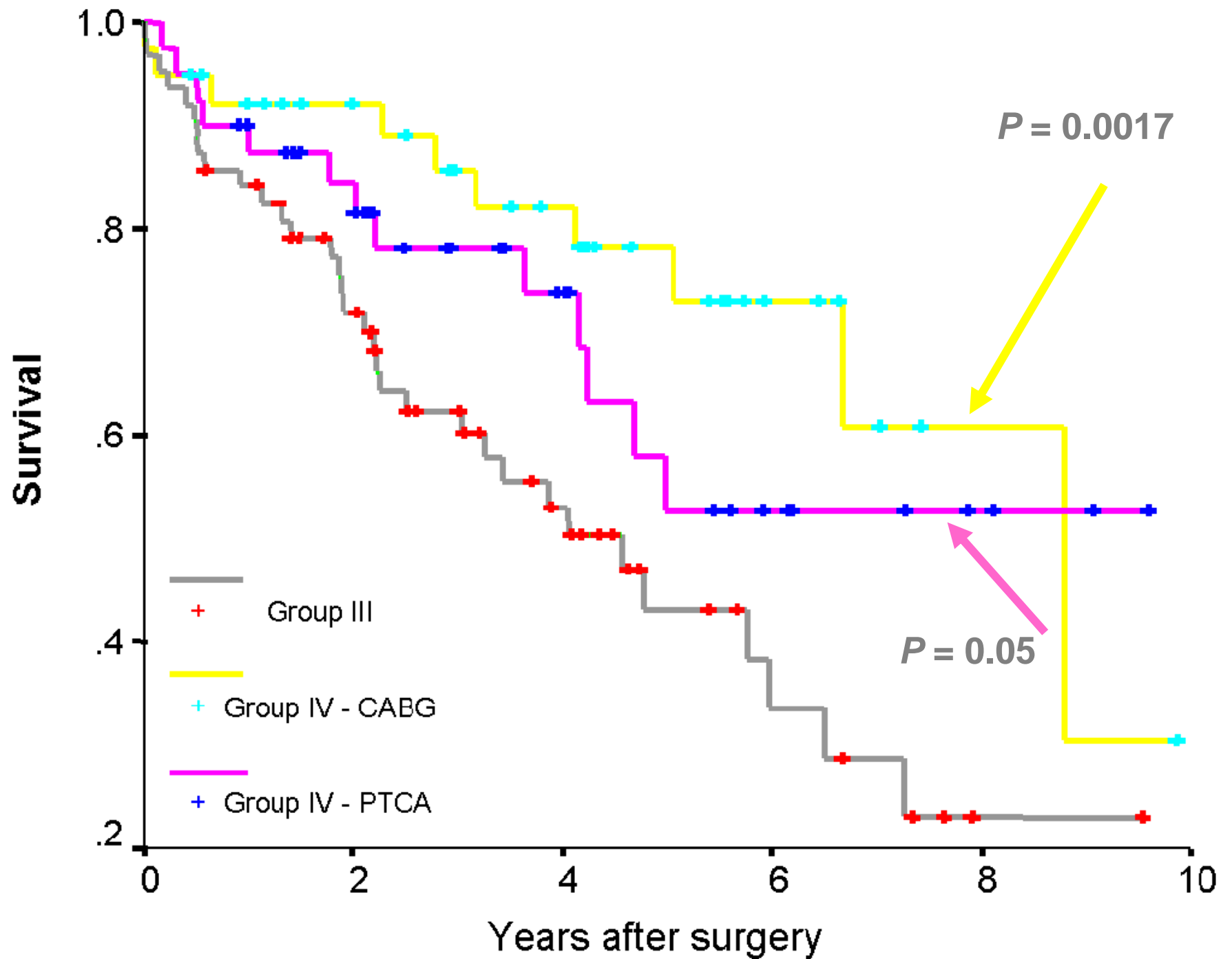
	Group III	Group IV	<i>P</i>
Preoperative coronary angiography	38 (61.3)	74 (100)	
Left main coronary stenosis (>50%)	3 (7.3)	15 (20.3)	0.058*
Triple-vessel disease (>70% stenosis)	15 (39.4)	41 (55.4)	0.11*
Double-vessel disease (>70% stenosis)	13 (34.2)	26 (35.1)	NS
Single-vessel disease (>70% stenosis)	6 (15.8)	7 (9.5)	NS
No significant coronary stenosis	4 (10.5)	0	NS
Preoperative LV function (by angiography or echocardiogram)	60 (96.7)	74 (100)	
Normal LV function	35 (58.3)	42 (56.8)	NS
Mildly reduced LV function	6 (10)	11 (14.9)	NS
Moderately reduced LV function	13 (21.7)	8 (10.8)	NS
Severely reduced LV function	6 (10)	13 (17.6)	NS

Values are n (%).

* $P=0.029$ for left main and triple-vessel disease combined.

Preoperative thallium and selective revascularization in 502 vascular patients





Conclusions

1. A significant proportion of patients undergoing vascular surgery had moderate-severe CAD, which was detectable by preoperative thallium scanning and treatable by coronary revascularization.

Conclusions

2. Coronary revascularization in these cohort of non-randomized patients was associated with improved long-term survival (odds ratio = 0.52)



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European Heart Journal (2007) 28, 533–539
doi:10.1093/eurheartj/ehl390

Clinical research
Coronary heart disease

A clinical survival score predicts the likelihood to benefit from preoperative thallium scanning and coronary revascularization before major vascular surgery

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We have constructed a Long-Term (3-15 yrs) Survival Score (LTSS) comprised of 7 independent predictors of survival;

Age ≥ 65

Diabetes

Renal insufficiency.

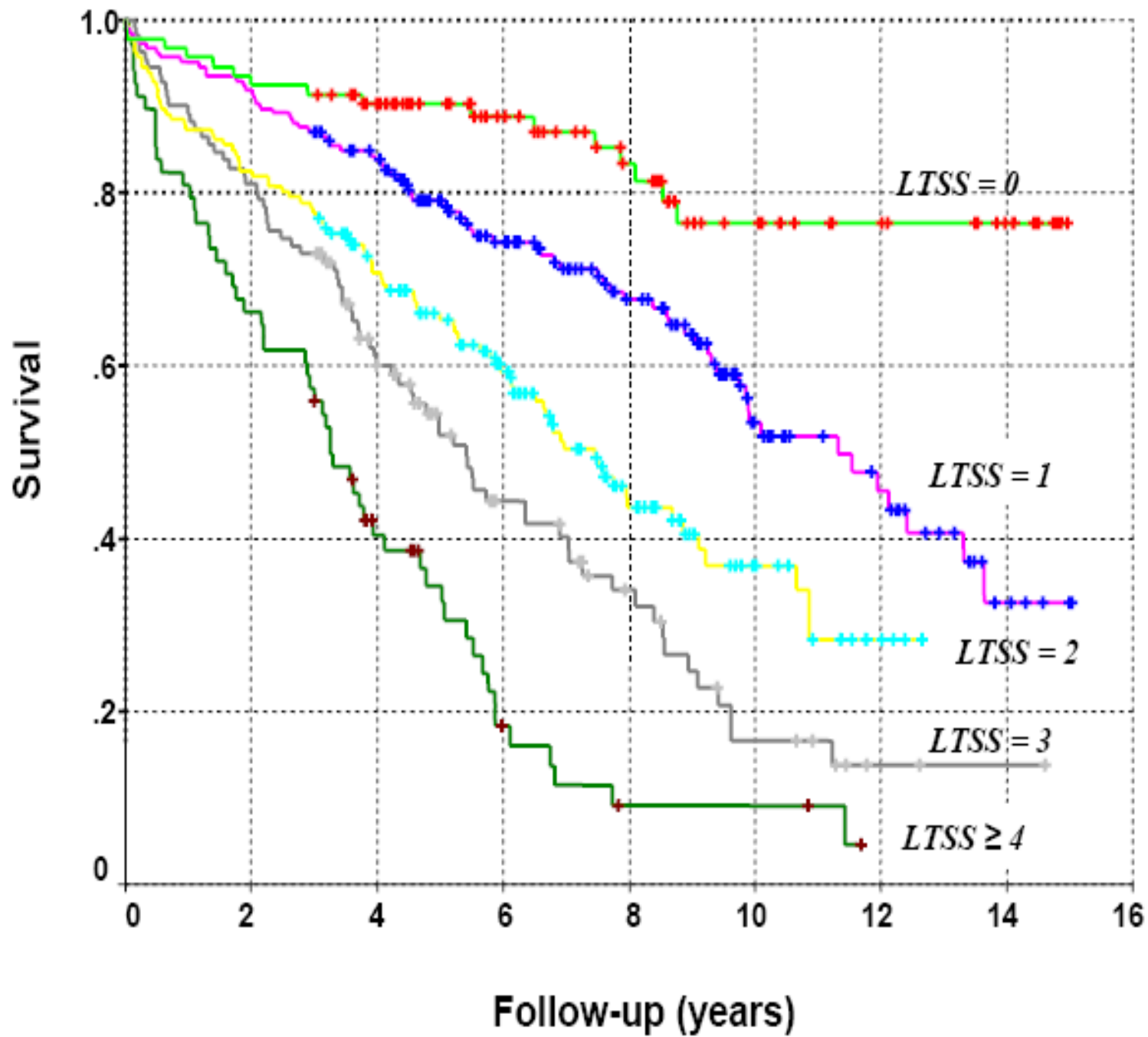
Ischemic heart disease

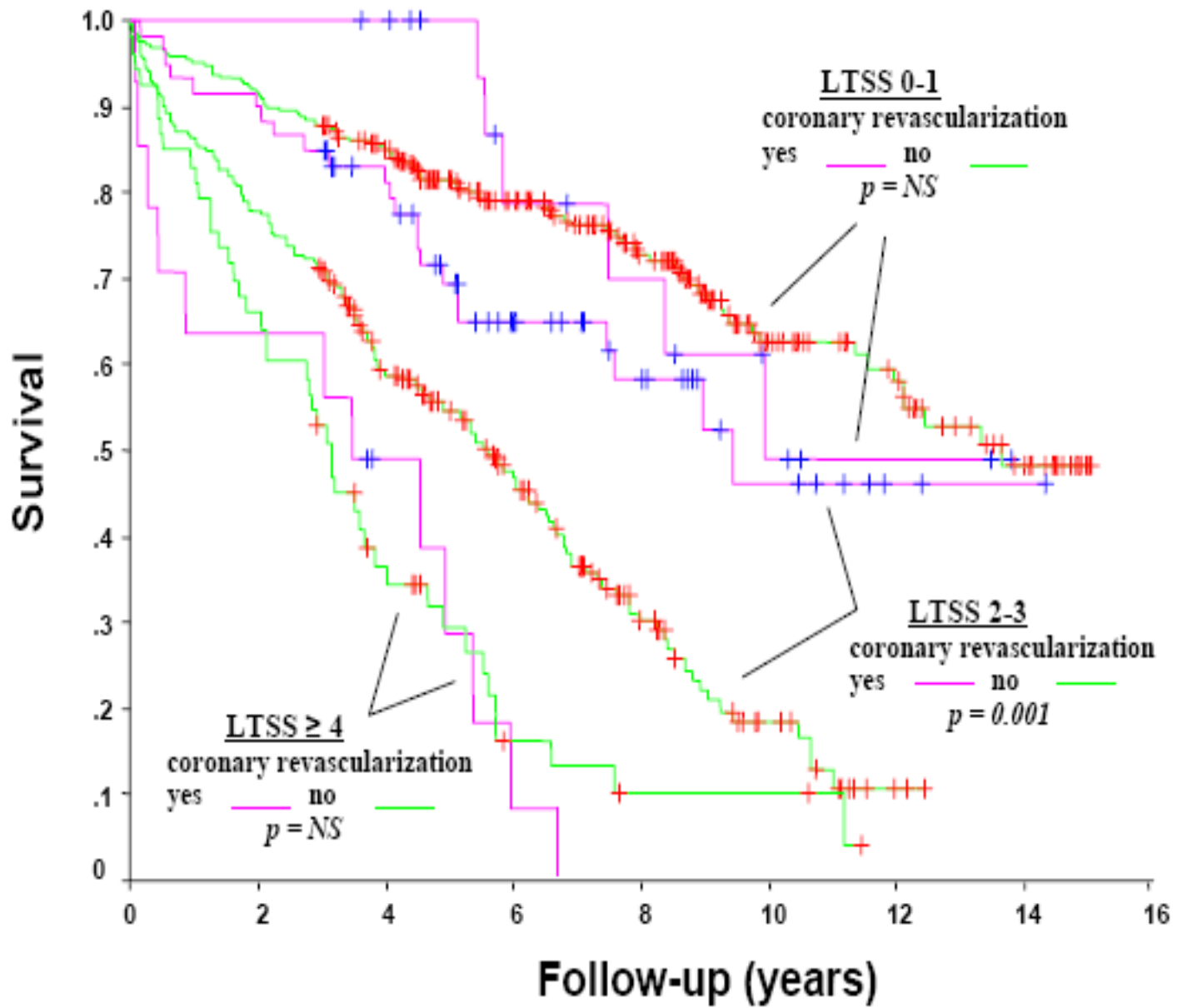
Congestive hear failure

Cerebrovascular disease

ST-depression on preoperative ECG

*Revised
Cardiac
Risk Index
(RCRI)*





Conclusions

Intermediate-risk patients (LTSS 2–3) are most likely to have a long-term survival benefit from PTS and CR.

Studies on PCI before noncardiac surgery

Table 10. Studies Reporting the Clinical Outcome of Patients Undergoing Noncardiac Surgery After a Percutaneous Coronary Intervention

Study Author	Year Published	No. of Patients who Underwent PCI	Time From PCI to Surgery	Perioperative Mortality, %	Perioperative Infarction Rate, %	Comments
Huber et al (179) Very high-risk patients, multivessel CAD	1992	50	9 days (mean)	1.9	5.6	CABG needed after balloon angioplasty in 10% of pts. No control group for comparison.
Elmore et al (180)	1993	<u>14</u>	10 days (mean)	0	0	Very small study. Event rate in pts. treated with CABG or balloon angioplasty less than in control group. Angioplasty pts. had fewer risk factors than pts. undergoing CABG.
Allen et al (181)	1991	148	338 days (mean)	2.7	0.7	<u>No increase in events if surgery performed within 90 days of PTCA.</u>
Gottlieb et al (296)	1998	<u>194</u>	11 days (median)	0.5	0.5	<u>Only vascular surgeries included.</u>
Possner et al (298) Case-control	1999	686	1 year (median)	2.6	2.2	Pts. who had undergone PCI had a similar frequency of death and MI but half the angina and HF of matched pts. with CAD who had not undergone PCI. Event rates were much higher if PCI had been performed within 90 days.
Kaluza et al (301)	2000	40	13 days (mean)	<u>20</u>	<u>16.8</u>	The only study in which stents were used. Mortality was 32% among pts. operated on less than 12 days after stent placement vs. 0 in pts. operated on 12 to 30 days after PCI.
Hassan et al (303) CABG = PTCA in periop. outcome	2001	251	29 months (median)	0.8	0.8	Among pts. who received PCI in BARI, outcome after noncardiac surgery was equivalent to that of BARI pts. who had received CABG.

Adopted from the ACC/AHA guidelines, update 2002

Were all these data just a reflection of selection bias?

or does prophylactic preoperative revascularization improve outcome?

Randomized controlled trials

**A Clinical Randomized Trial to Evaluate
the Safety of a Noninvasive Approach in
High-Risk Patients Undergoing Major Vascular Surgery**

The DECREASE-V Pilot Study *Poldermans et al. JACC 2007;49:1763-9*

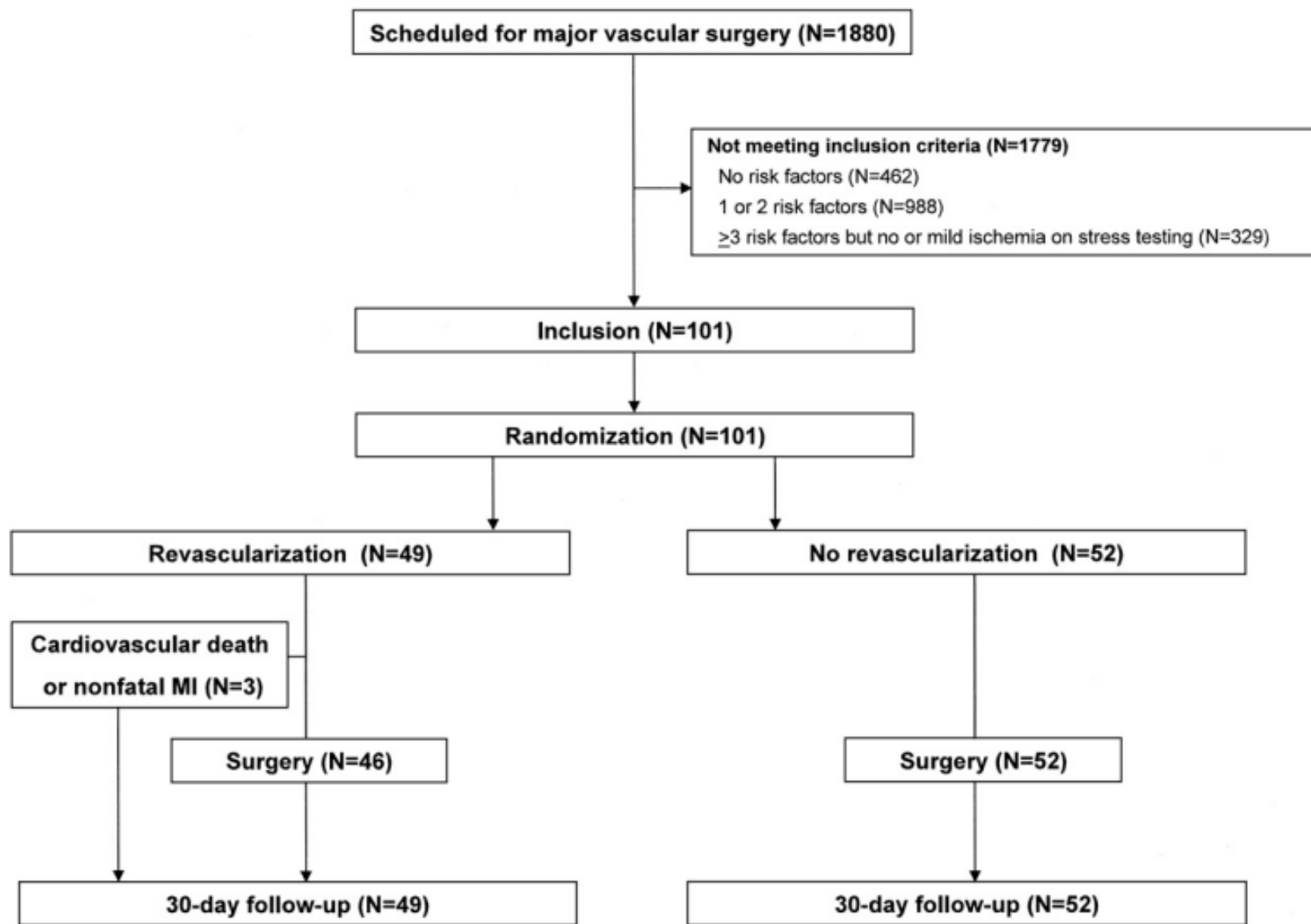


Figure 1 Flowchart of the Study

Cardiac risk factors included age over 70 years, angina pectoris, prior myocardial infarction (MI) on the basis of history or a finding of pathologic Q waves on electrocardiography, compensated congestive heart failure or a history of congestive heart failure, current treatment for diabetes mellitus, renal dysfunction (serum creatinine >160 $\mu\text{mol/l}$), and prior stroke or transient ischemic attack. Patients with >3 risk factors and extensive ischemia were randomly (1:1) assigned to coronary revascularization.

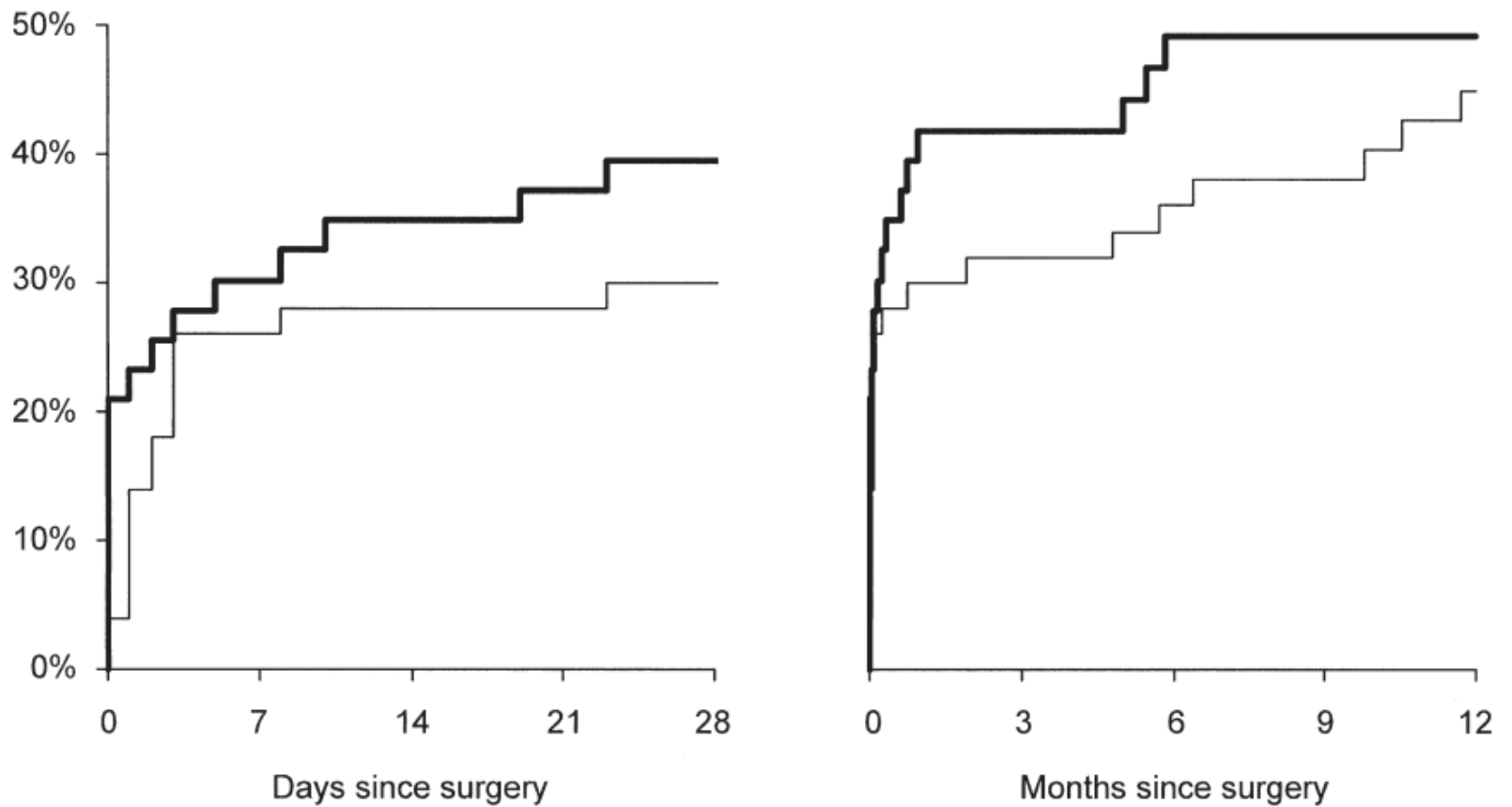


Figure 2

Incidence of All-Cause Death or Myocardial Infarction During 1-Year Follow-Up According to the Allocated Strategy in Patients With 3 or More Cardiac Risk Factors With Extensive Stress-Induced Ischemia

Light line = best medical treatment only; **dark line** = best medical treatment and prophylactic revascularization.

Investigators' conclusions

- Preoperative coronary revascularization in high-risk patients was not associated with an improved outcome.

Commentary

- Number of pts randomized: 101 (5.3%) of 1880 pts screened.
- All 101 pts with extensive ischemia were randomized before angiography.
- Pts in the revascularization group had extremely high 30-day mortality after vascular surgery (22% vs. 11%) despite successful and complete revascularization (86%) !
- Postoperative MI rate was dreadfully high: 35% vs. 31% and all were Q-wave MI's !

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

DECEMBER 30, 2004

VOL. 351 NO. 27

Coronary-Artery Revascularization before Elective Major Vascular Surgery

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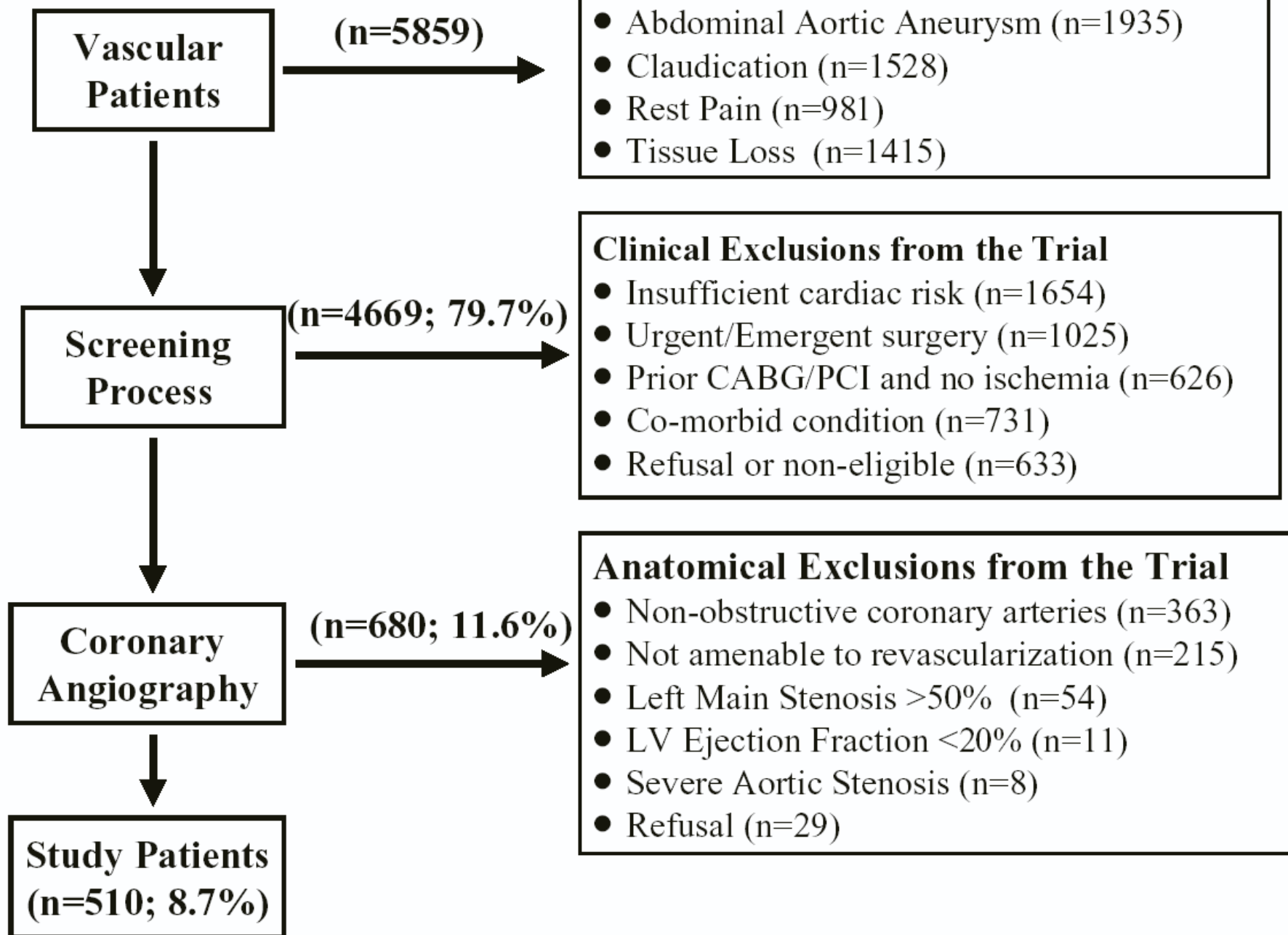
The CARP study

Patients

Inclusion criteria - pts scheduled for an elective vascular surgery for either AAA or severe symptoms of arterial occlusive disease involving the legs.

Exclusion criteria - a need for urgent or emergency surgery, a severe coexisting illness, or prior revascularization without evidence of recurrent ischemia.

Figure 1: Study Registry



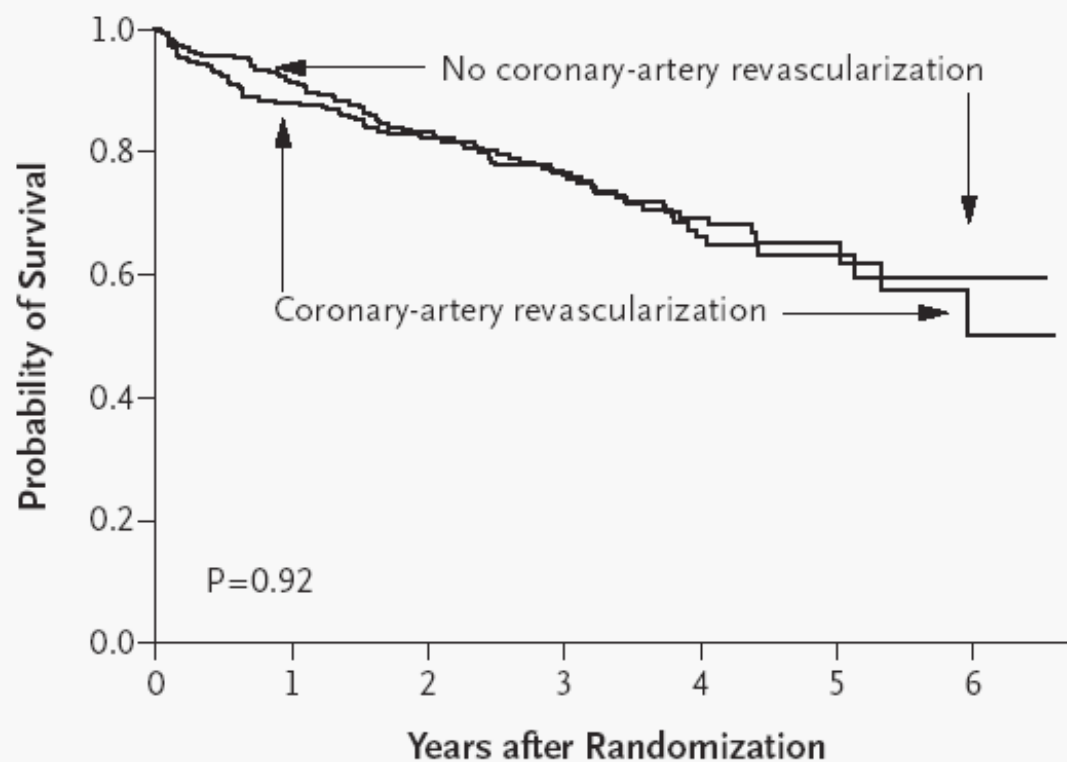
Study protocol

Coronary angiography was recommended if the patient was considered to be at increased risk for a peri-operative cardiac complication on the basis of combined clinical risk factors and the presence of ischemia on a noninvasive stress imaging study.

Local investigators decided which revascularization procedure to use, either PCI or CABG.

The primary end point was long-term mortality.

Secondary end points included myocardial infarction, stroke, limb loss, and dialysis.



No. at Risk

Revascularization	226	175	113	65	18	7
No revascularization	229	172	108	55	17	12

Figure 1. Long-Term Survival among Patients Assigned to Undergo Coronary-Artery Revascularization or No Coronary-Artery Revascularization before Elective Major Vascular Surgery.

Kaplan–Meier estimates were used to generate survival curves, from the time of randomization, for all study patients.

Investigators' conclusions

“Among patients with stable CAD, coronary revascularization before elective major vascular surgery does not improve *long-term* survival.”

“There was no reduction in early *postoperative outcomes*, including death, myocardial infarction, and length of the hospital stay.”

“CABG or PCI should be reserved for pts with unstable cardiac symptoms or advanced coronary artery disease, for whom a survival benefit with CABG has been proved.”

Commentary

- Only a small proportion (8.9%) of screened patients was randomized.
- Only 44% of randomized patients had moderate-large ischemia on preoperative nuclear imaging.
- Only 32% had TVD (2.9% of all screened patients), indicating a potential selection bias with the possibility that mainly patients less likely to benefit from pre-operative revascularization were included in the trial.
- Patients with left-main CAD were excluded by-design from randomization.

Usefulness of Revascularization of Patients With Multivessel Coronary Artery Disease Before Elective Vascular Surgery for Abdominal Aortic and Peripheral Occlusive Disease

Santiago Garcia, MD^a, Thomas E. Moritz, MS^b, Herbert B. Ward, MD, PhD^a,
Gordon Pierpont, MD, PhD^a, Steve Goldman, MD^d, Greg C. Larsen, MD^e, Fred Littooy, MD^e,
William Krupski, MD^{f,†}, Lizy Thottapurathu, MS^b, Domenic J. Reda, PhD^b, and
Edward O. McFalls, MD, PhD^{a,*}

The Coronary Artery Revascularization Prophylaxis (CARP) study showed no survival benefit with preoperative coronary artery revascularization before elective vascular surgery. The generalizability of the trial results to all patients with multivessel coronary artery disease (CAD) has been questioned. The objective of this study was to determine the impact of prophylactic coronary revascularization on long-term survival in patients with multivessel CAD. Over a 4-year period, 1,048 patients underwent coronary angiography before vascular surgery during screening into the CARP trial. The cohort was composed of registry (n 586) and randomized (n 462) patients, and their survival was determined at 2.5 years after vascular surgery. High-risk coronary anatomy without previous bypass surgery included 2-vessel disease (n 304, [19.5%]), 3-vessel disease (n 130, [12.4%]), and left main coronary artery stenosis $\geq 50\%$ (n 48, [4.6%]). By log-rank test, preoperative revascularization was associated with improved survival in patients with a left main coronary artery stenosis (0.84 vs 0.52, $p < 0.01$) but not those with either 2-vessel (0.80 vs 0.79, $p = 0.83$) or 3-vessel (0.79 vs 0.71, $p = 0.15$) disease. In conclusion, unprotected left main coronary artery disease was present in 4.6% of patients who underwent coronary angiography before vascular surgery, and this was the only subset of patients showing a benefit with preoperative coronary artery revascularization. © 2008 Elsevier Inc. All rights reserved. (Am J Cardiol 2008;102:809 – 813)

Conclusions

- Unprotected left main coronary artery disease was present in 4.6% of patients who underwent coronary angiography before vascular surgery and this subset of patients showed a benefit from coronary artery revascularization.

CLINICAL RESEARCH

Clinical Trial

Systematic Strategy of Prophylactic Coronary Angiography Improves Long-Term Outcome After Major Vascular Surgery in Medium- to High-Risk Patients

A Prospective, Randomized Study

Mario Monaco, MD,* Paolo Stassano, MD,‡ Luigi Di Tommaso, MD,‡ Paolo Pepino, MD,*
Arturo Giordano, MD,† Giovanni B. Pinna, MD,‡ Gabriele Iannelli, MD,‡
Giuseppe Ambrosio, MD, PhD§

Castelvolturmo, Naples, and Perugia, Italy

Methods

- Patients: 208 consecutive patients scheduled for elective surgical treatment of major vascular disease and with a revised cardiac risk index ≥ 2 .
- Randomization: Patients were allocated to either a “selective strategy” group (group A, n=103), in whom coronary angiography was performed based on the results of noninvasive tests, or to a “systematic strategy” group (group B, n=105), consisting of patients who systematically underwent pre-operative coronary angiography with no preceding non-invasive tests.

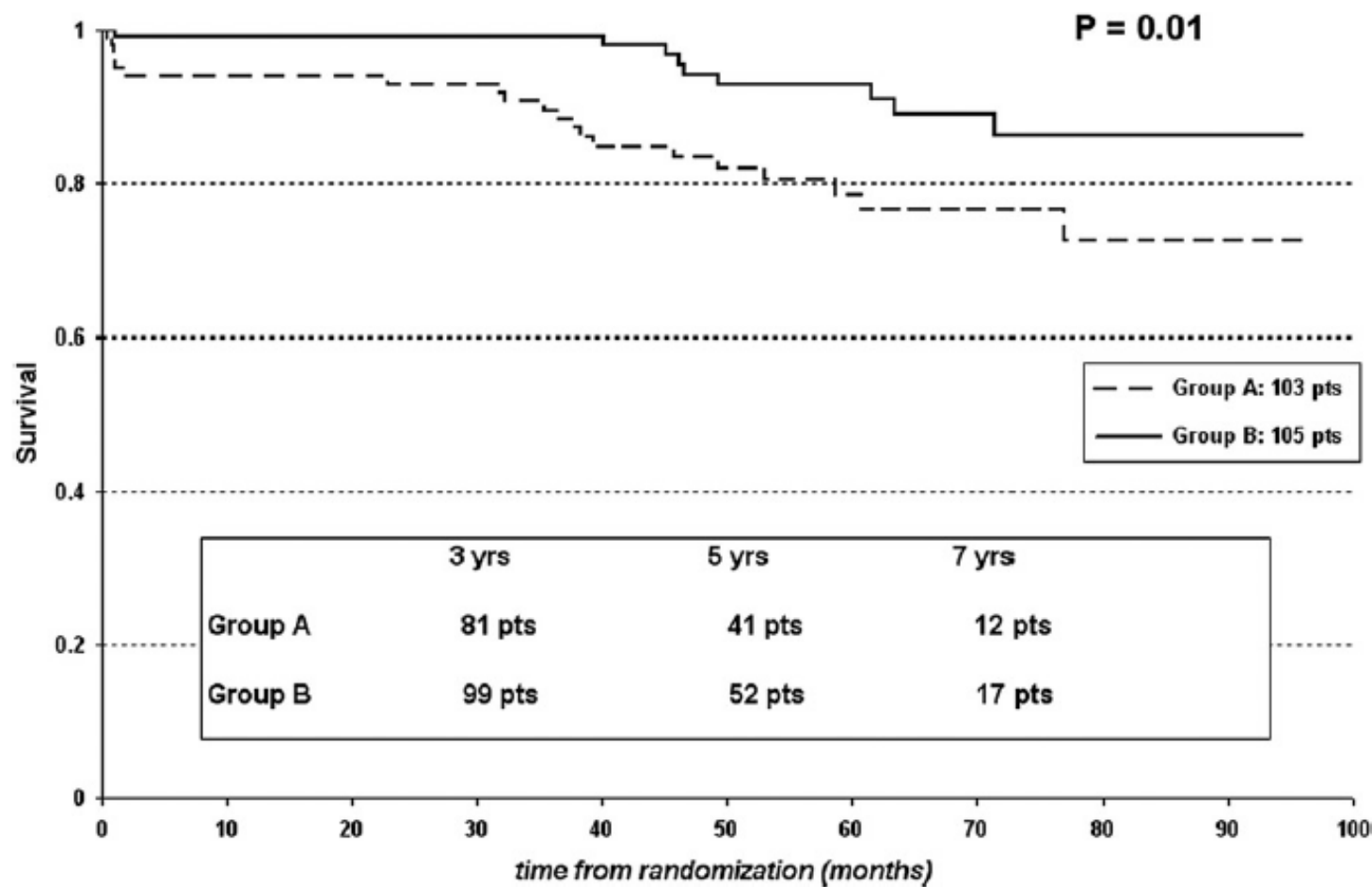


Figure 1 Cumulative Survival

Cumulative survival for patients (pts) of group A (**dashed line** [n = 103]) and group B (**solid line** [n = 105]), intention-to-treat.

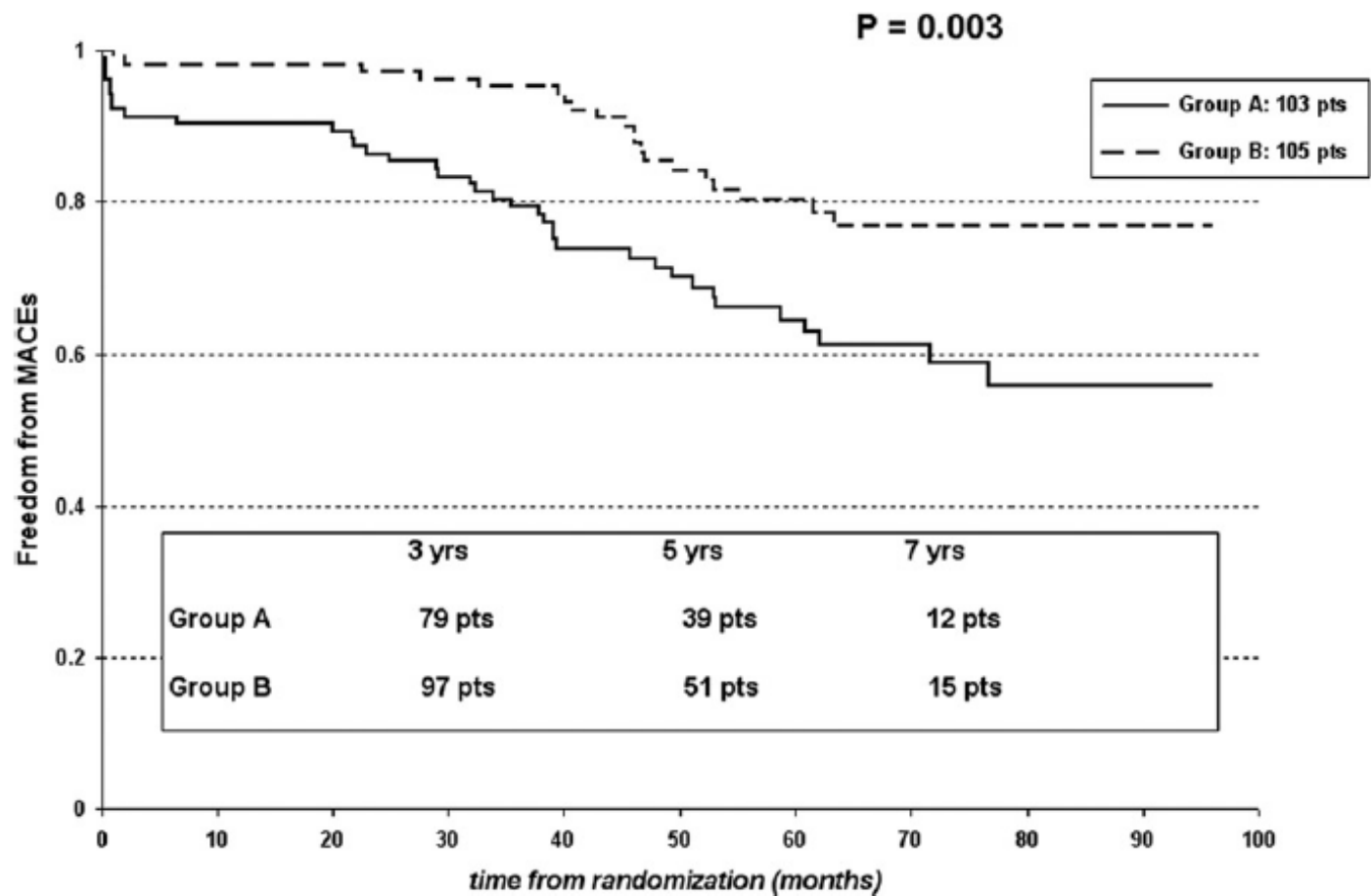


Figure 2 Freedom From Major Cardiac Events

Freedom from major adverse cardiac events (MACE) for patients (pts) of group A (**solid line** [n = 103]) and group B (**dashed line** [n = 105]), intention-to-treat.

Differences between Monaco's and CARP and DECREASE RCT's

The surgery:

- Monaco's trial included only patients who underwent abdominal aortic surgery - a procedure with increased left ventricular afterload during aortic clamping.

The patients:

- Compared to the CARP trial, Monaco patients had more extensive CAD, including left main disease and higher prevalence of TVD.
- On the other hand, DECREASE-V patients were much sicker than Monaco's with more cardiac and noncardiac co-morbidities and had poorer prognosis regardless of any preoperative treatment.

It is possible that Monaco et al have identified a specific subset of patients who might benefit from pre-operative revascularization prior to vascular surgery.

Differences between Monaco's RCT and the others

- **Myocardial revascularization:**
 - Patients in the systematic preoperative coronary angiography group underwent more OPCAB than PCI, compared with the control group (47.5% vs. 28.6%, respectively with a tendency for statistical significance $p=0.08$).

It is likely that more patients with left main disease or TVD in the systematic angiography group underwent pre-operative revascularization.

(Do patients with PVD and TVD have false negative non-invasive testing?) .

Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery

The Task Force for Preoperative Cardiac Risk Assessment and Perioperative Cardiac Management in Non-cardiac Surgery of the European Society of Cardiology (ESC) and endorsed by the European Society of Anaesthesiology (ESA)

Authors/Task Force Members: Don Poldermans; (Chairperson) (The Netherlands)*; Jeroen J. Bax (The Netherlands); Eric Boersma (The Netherlands); Stefan De Hert (The Netherlands); Erik Eeckhout (Switzerland); Gerry Fowkes (UK); Bulent Gorenek (Turkey); Michael G. Hennerici (Germany); Bernard Jung (France); Malte Kelm (Germany); Keld Per Kjeldsen (Denmark); Steen Dalby Kristensen (Denmark); Jose Lopez-Sendon (Spain); Paolo Pelosi (Italy); François Philippe (France); Luc Pierard (Belgium); Piotr Ponikowski (Poland); Jean-Paul Schmid (Switzerland); Olav F.M. Sellevold (Norway); Rosa Sicari (Italy); Greet Van den Berghe (Belgium); Frank Vermassen (Belgium)

Additional Contributors: Sanne E. Hoeks (The Netherlands); Ilse Vanhorebeek (Belgium)

ESC Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery

Angiography

- There is a lack of information derived from randomized clinical trials on its usefulness in patients scheduled for non-cardiac surgery.
- Nevertheless, IHD may be present in a significant number of patients in whom non-cardiac surgery is indicated.

ESC Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery

Angiography

- In patients with known IHD, indications for pre-operative coronary angiography and revascularization are similar to angiography indications in the non-surgical setting.
- The control of ischemia before surgery, either medically or with intervention, is recommended whenever non-cardiac surgery procedures can be delayed.

Recommendations on pre-operative coronary angiography

Recommendations	Class ^a	Level ^b
Pre-operative angiography is recommended in patients with acute STEMI	I	A
Pre-operative angiography is recommended in patients with NSTEMI and unstable angina	I	A
Pre-operative angiography is recommended in patients with angina not controlled with adequate medical therapy	I	A
Pre-operative angiography may be considered in cardiac-stable patients undergoing high-risk surgery	IIb	B
Pre-operative angiography may be considered in cardiac-stable patients undergoing intermediate-risk surgery	IIb	C
Pre-operative angiography is not recommended in cardiac-stable patients undergoing low-risk surgery	III	C

^aClass of recommendation.

^bLevel of evidence.

STEMI – ST-segment elevation myocardial infarction; NSTEMI – non-ST-segment elevation myocardial infarction.

ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Non-Cardiac Surgery

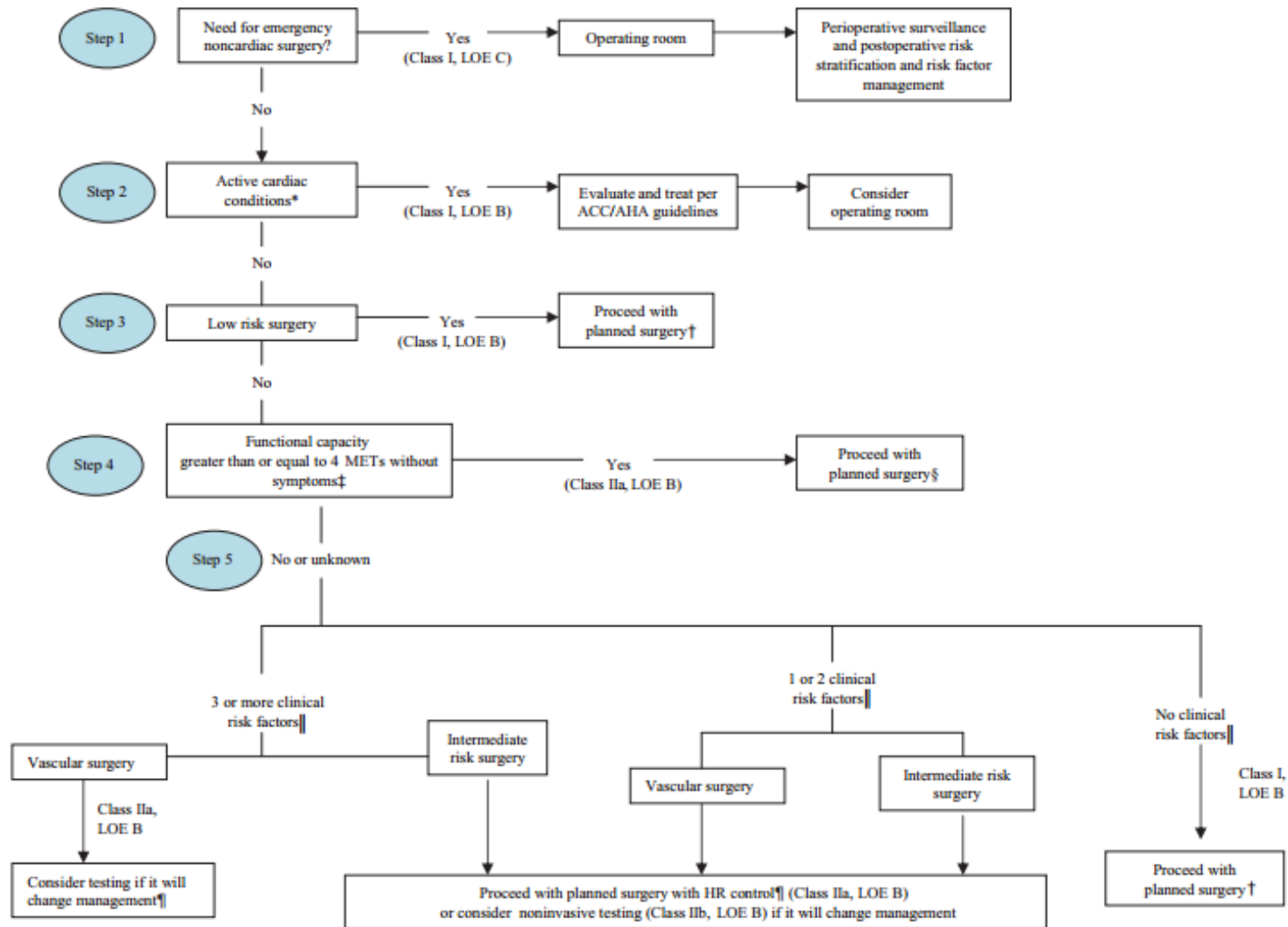
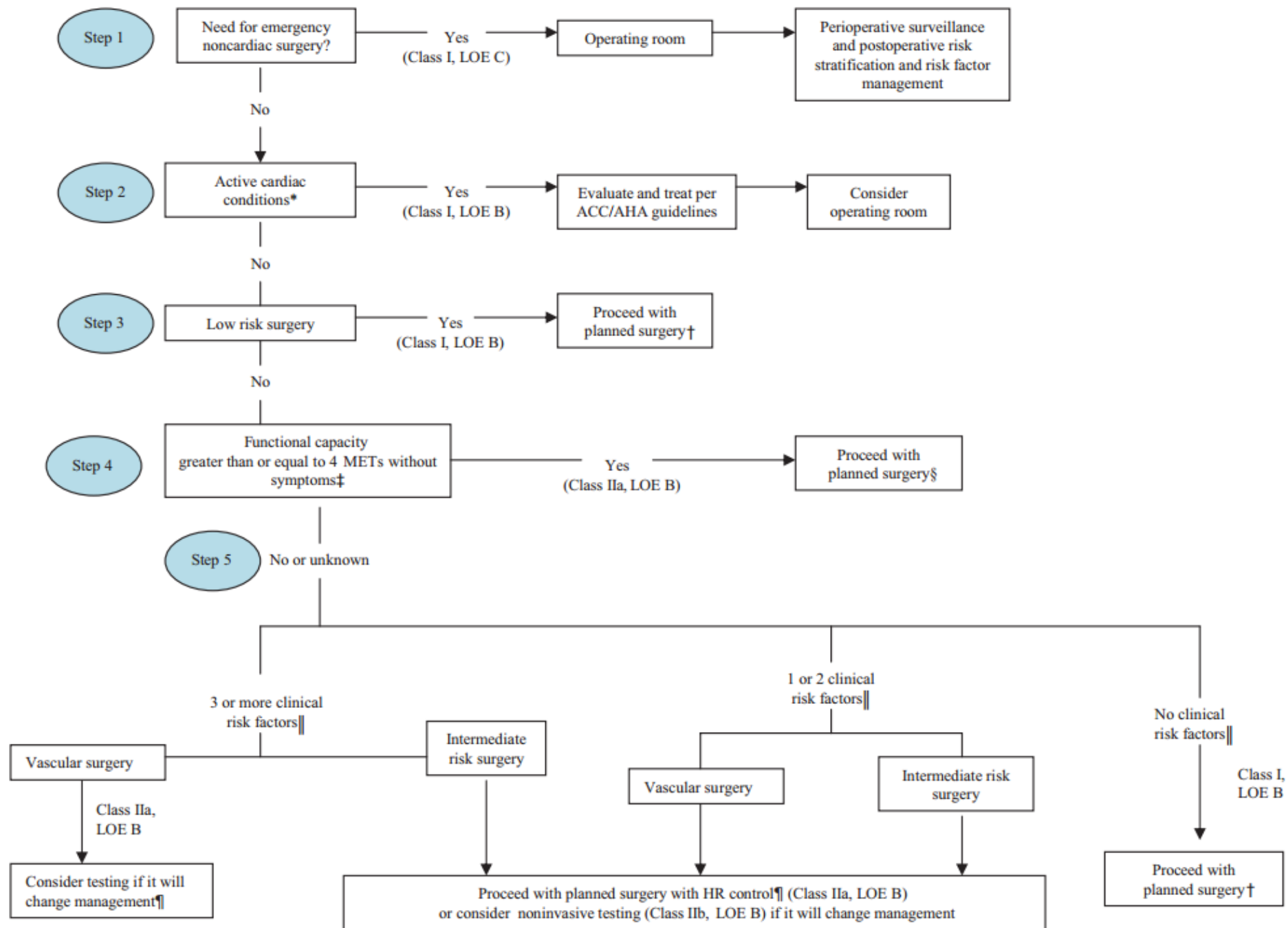


Figure 1. Cardiac evaluation and care algorithm for noncardiac surgery based on active clinical conditions, known cardiovascular disease, or cardiac risk factors for patients 50 years of age or greater. *See Table 2 for active clinical conditions. †See Class III recommendations in Section 5.2.3. Noninvasive Stress Testing. ‡See Table 3 for estimated MET level equivalent. §Noninvasive testing may be considered before surgery in specific patients with risk factors if it will change management. ||Clinical risk factors include ischemic heart disease, compensated or prior heart failure, diabetes mellitus, renal insufficiency, and cerebrovascular disease. ¶Consider perioperative beta blockade (see Table 12) for populations in which this has been shown to reduce cardiac morbidity/mortality. ACC/AHA indicates American College of Cardiology/American Heart Association; HR, heart rate; LOE, level of evidence; and MET, metabolic equivalent.



Step 1

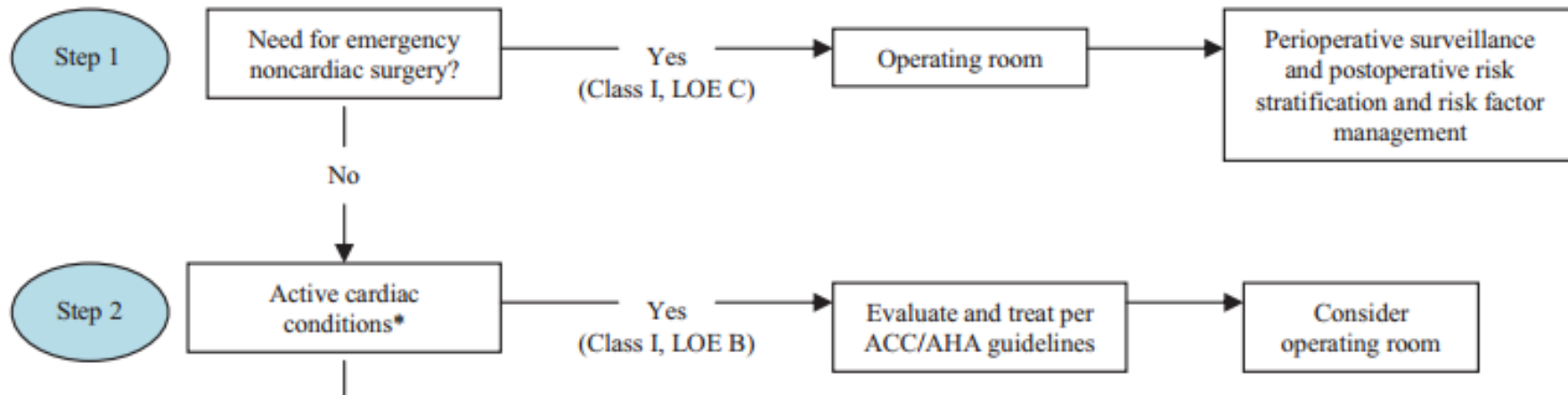
Need for emergency
noncardiac surgery?

Yes
(Class I, LOE C)

Operating room

Perioperative surveillance
and postoperative risk
stratification and risk factor
management





- unstable coronary syndromes,
 - unstable or severe angina,
 - recent MI,
- decompensated HF,
- significant arrhythmias, and
- severe valvular disease.

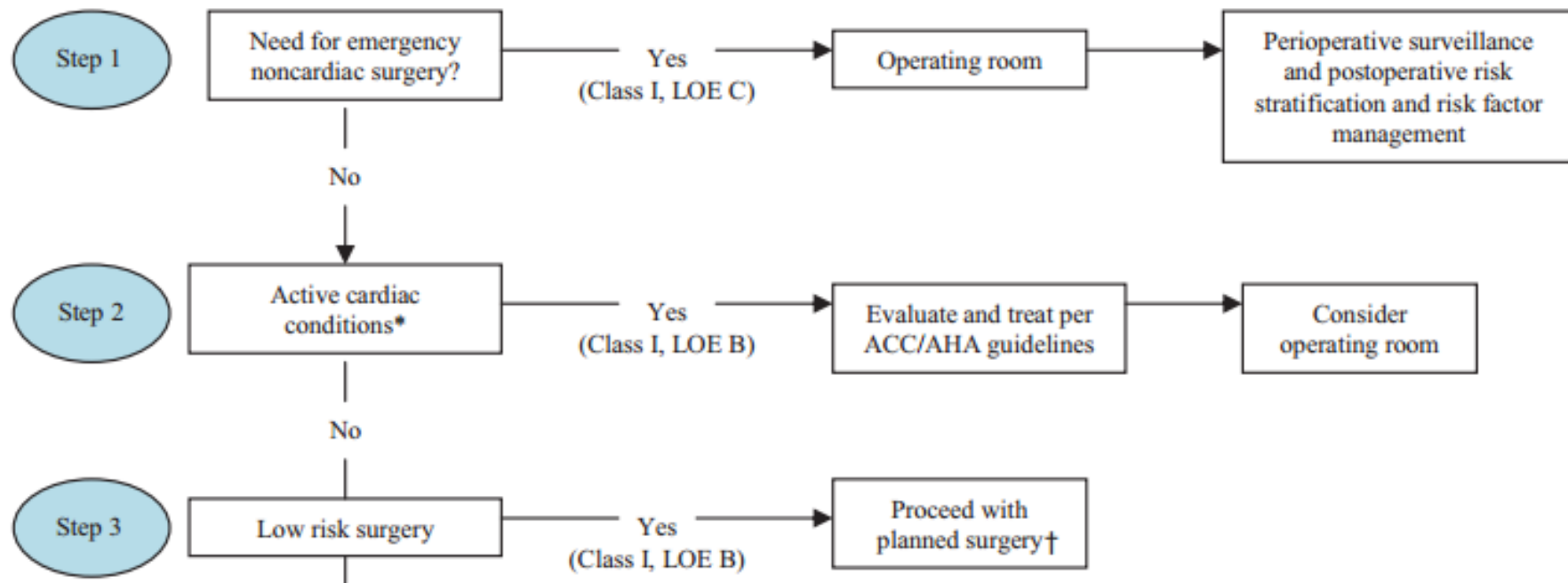
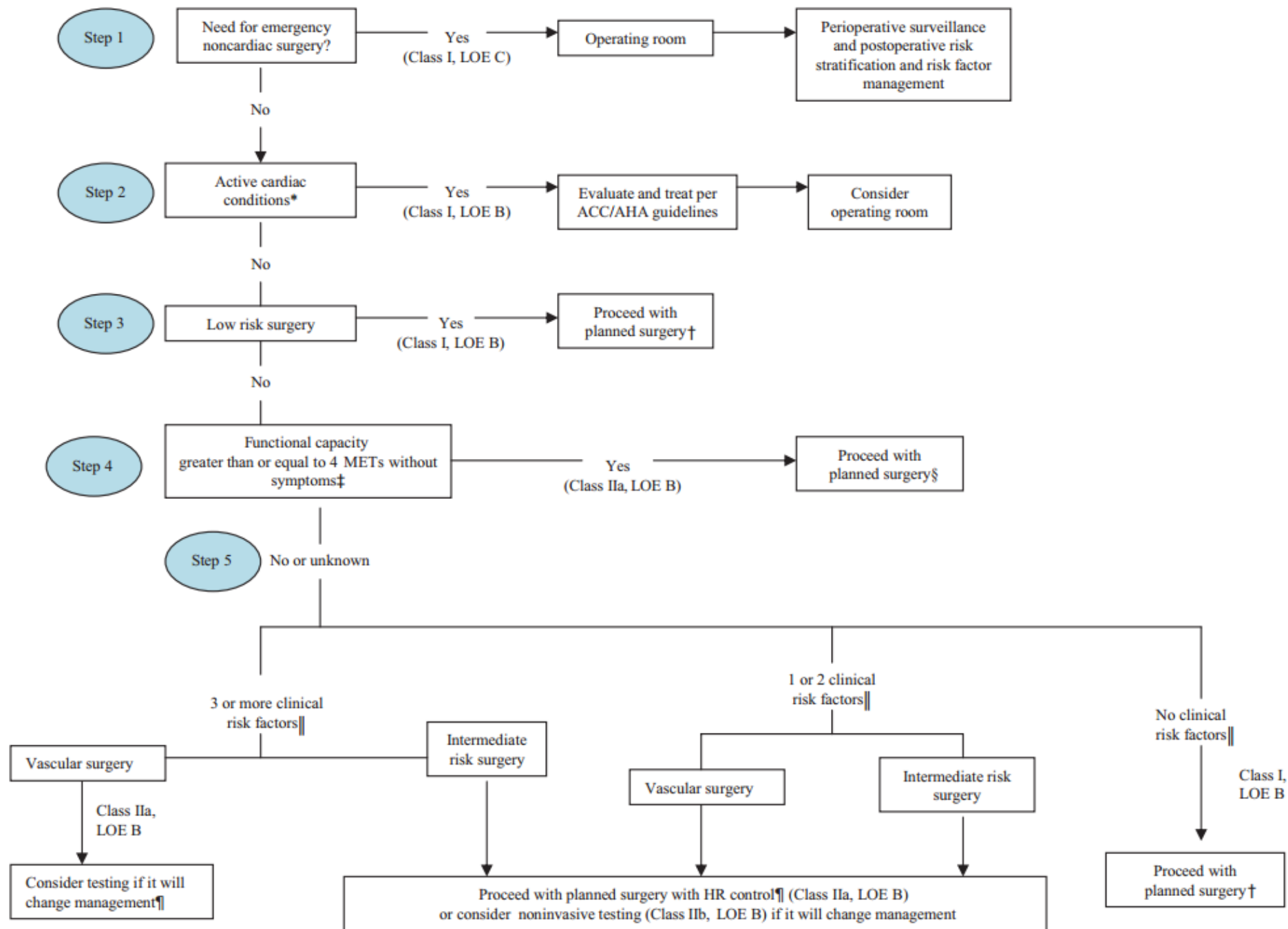


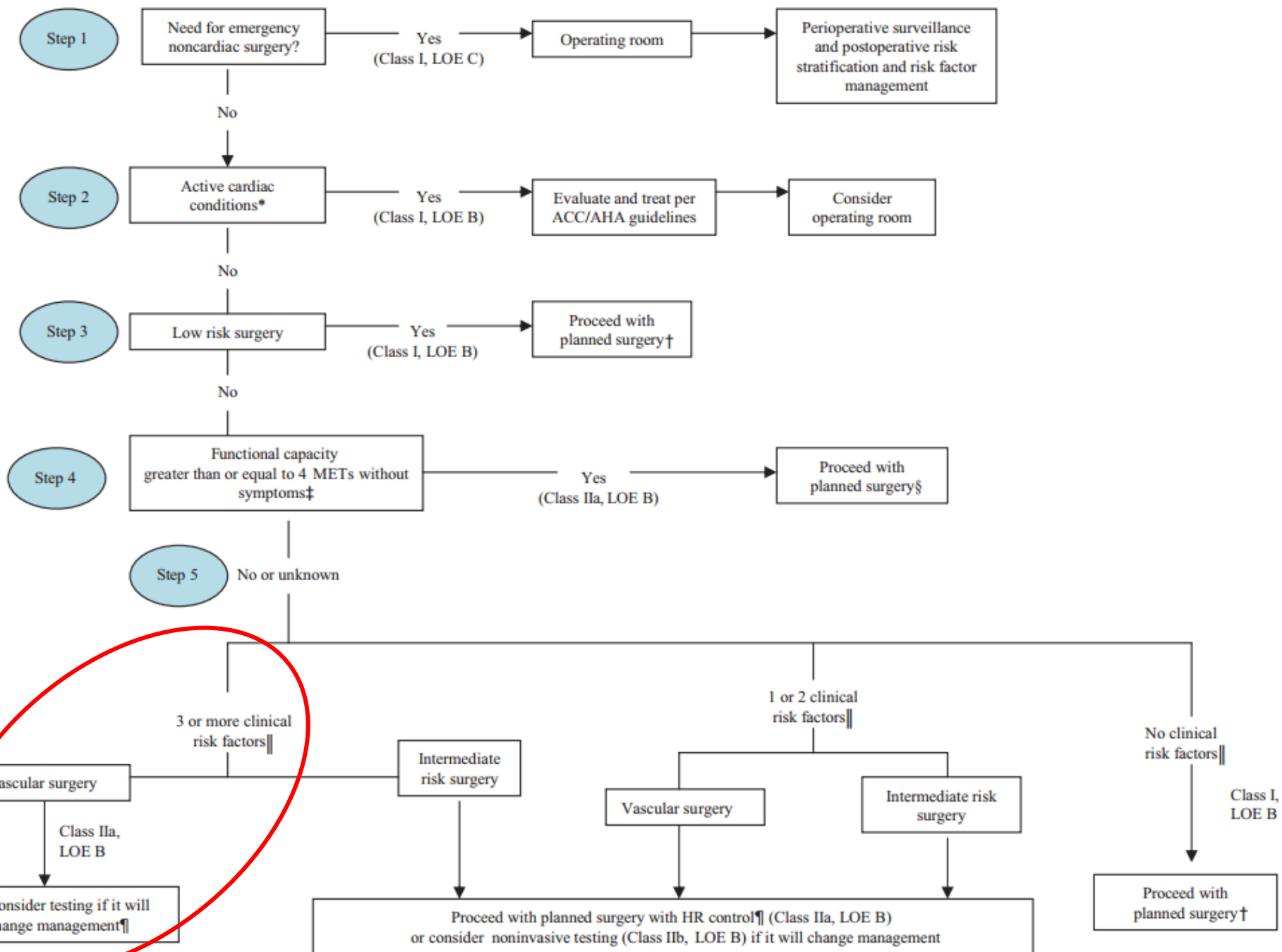
Table 3. Estimated Energy Requirements for Various Activities

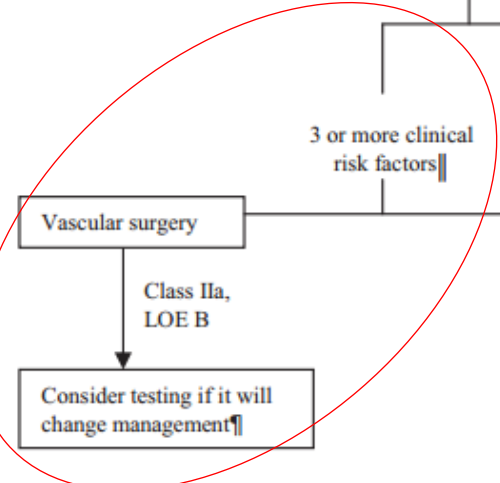
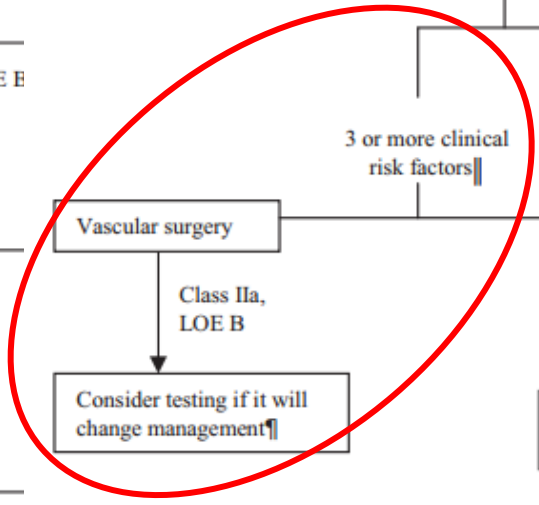
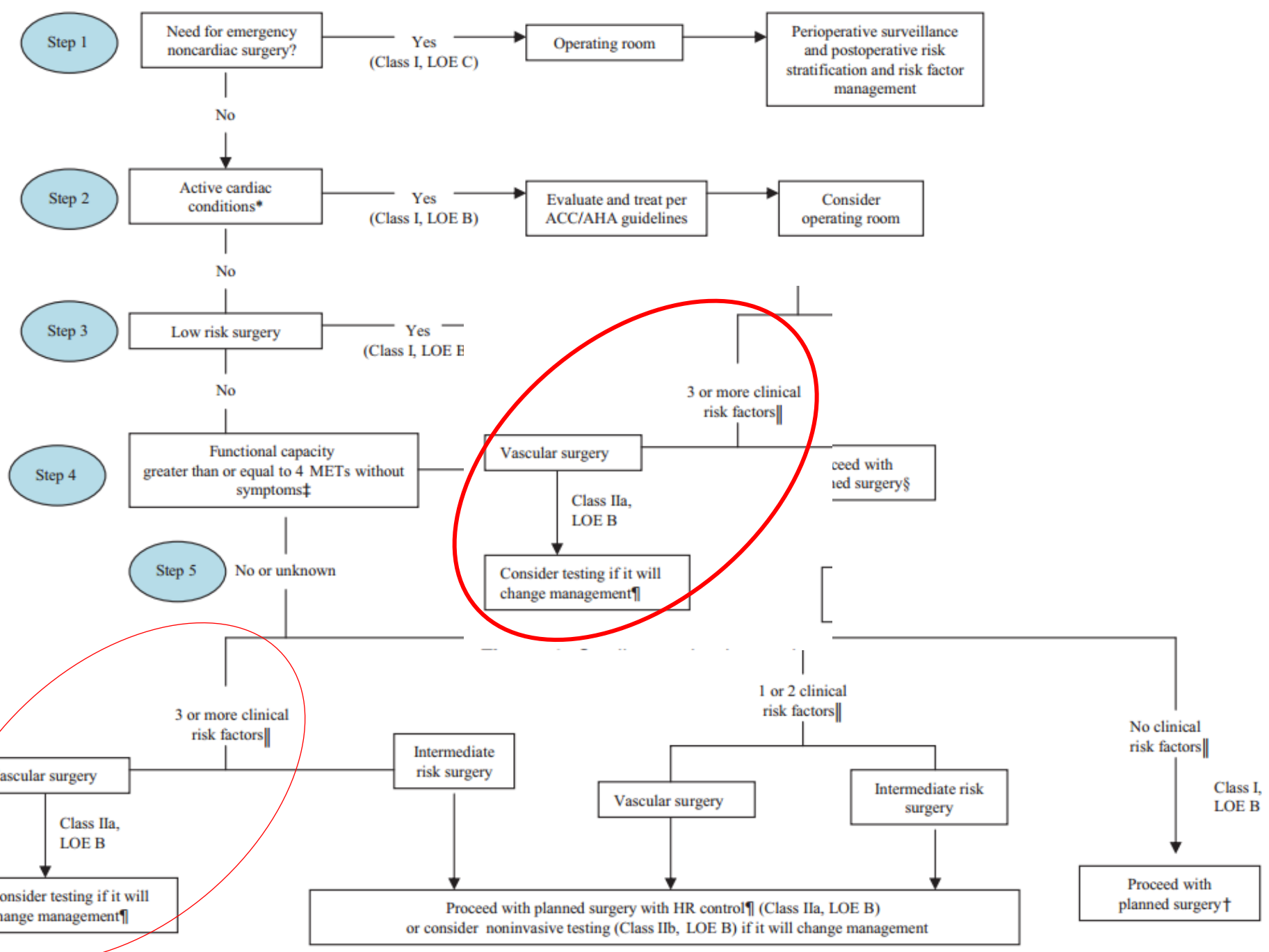
1 MET	Can you ... Take care of yourself?	4 METs	Can you ... Climb a flight of stairs or walk up a hill?
	Eat, dress, or use the toilet?		Walk on level ground at 4 mph (6.4 kph)?
	Walk indoors around the house?		Run a short distance?
	Walk a block or 2 on level ground at 2 to 3 mph (3.2 to 4.8 kph)?		Do heavy work around the house like scrubbing floors or lifting or moving heavy furniture?
4 METs	Do light work around the house like dusting or washing dishes?		Participate in moderate recreational activities like golf, bowling, dancing, doubles tennis, or throwing a baseball or football?
		Greater than 10 METs	Participate in strenuous sports like swimming, singles tennis, football, basketball, or skiing?

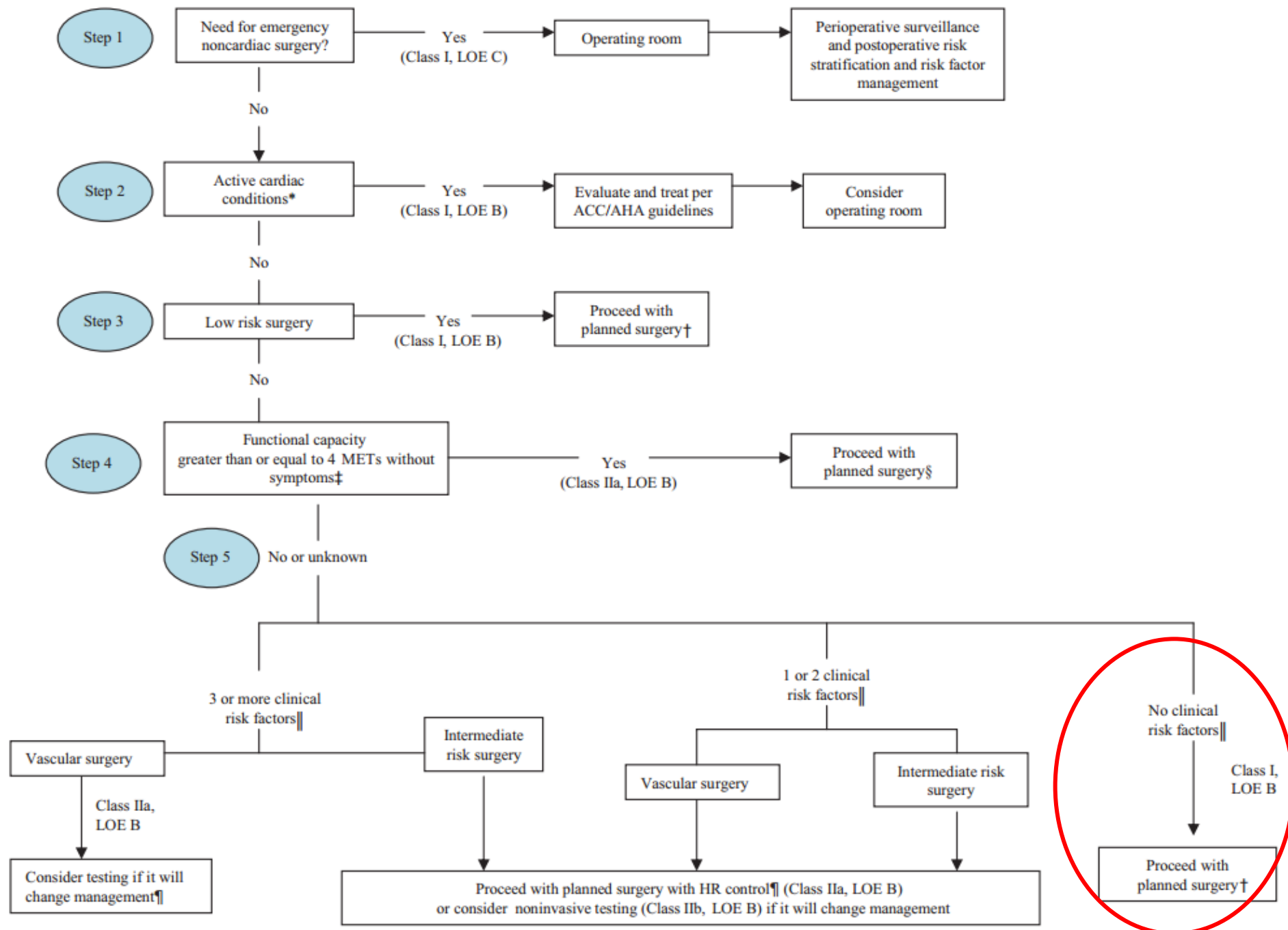
kph indicates kilometers per hour; MET, metabolic equivalent; and mph, miles per hour.

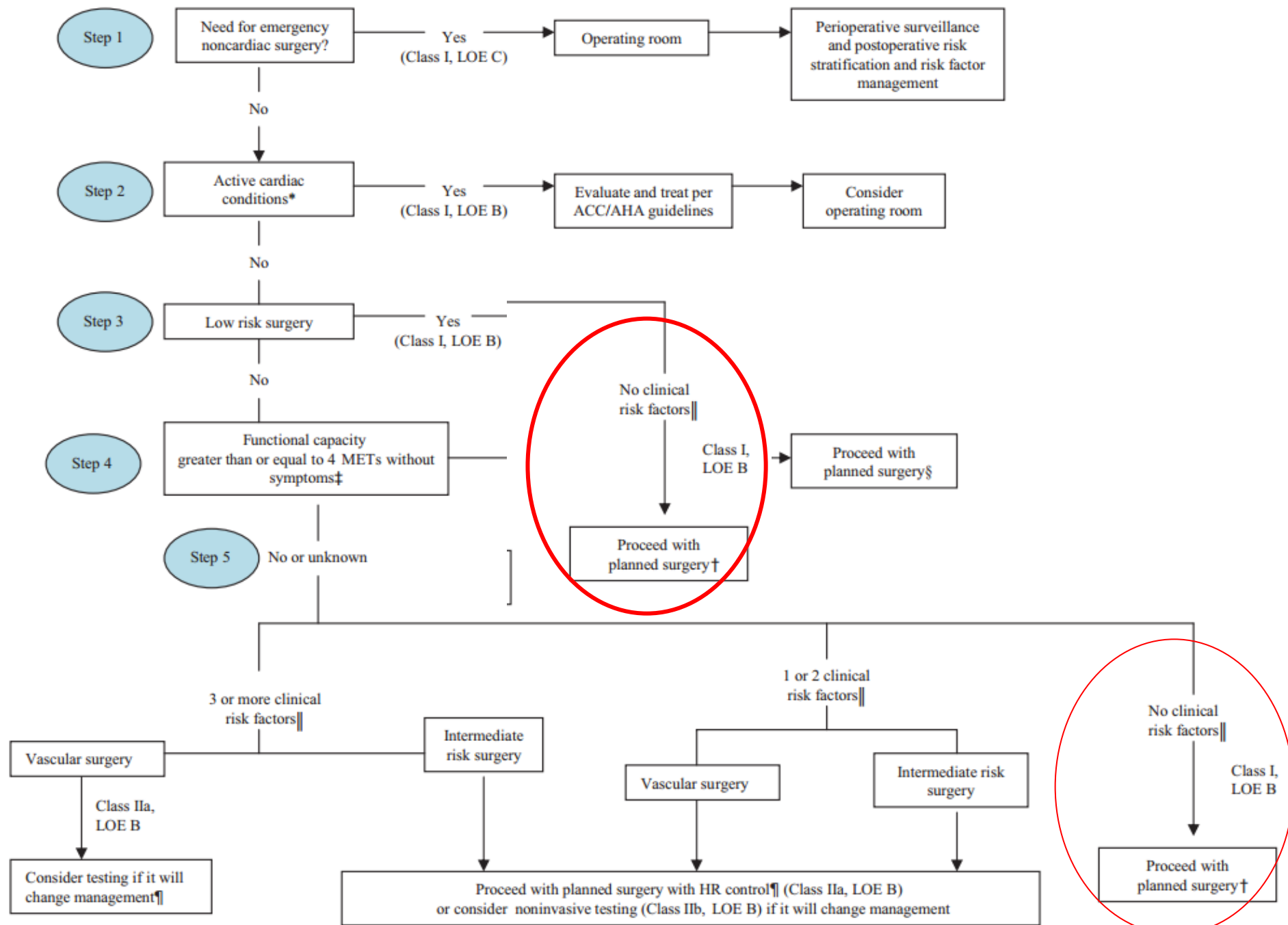
*Modified from Hlatky et al,¹¹ copyright 1989, with permission from Elsevier, and adapted from Fletcher et al.¹²

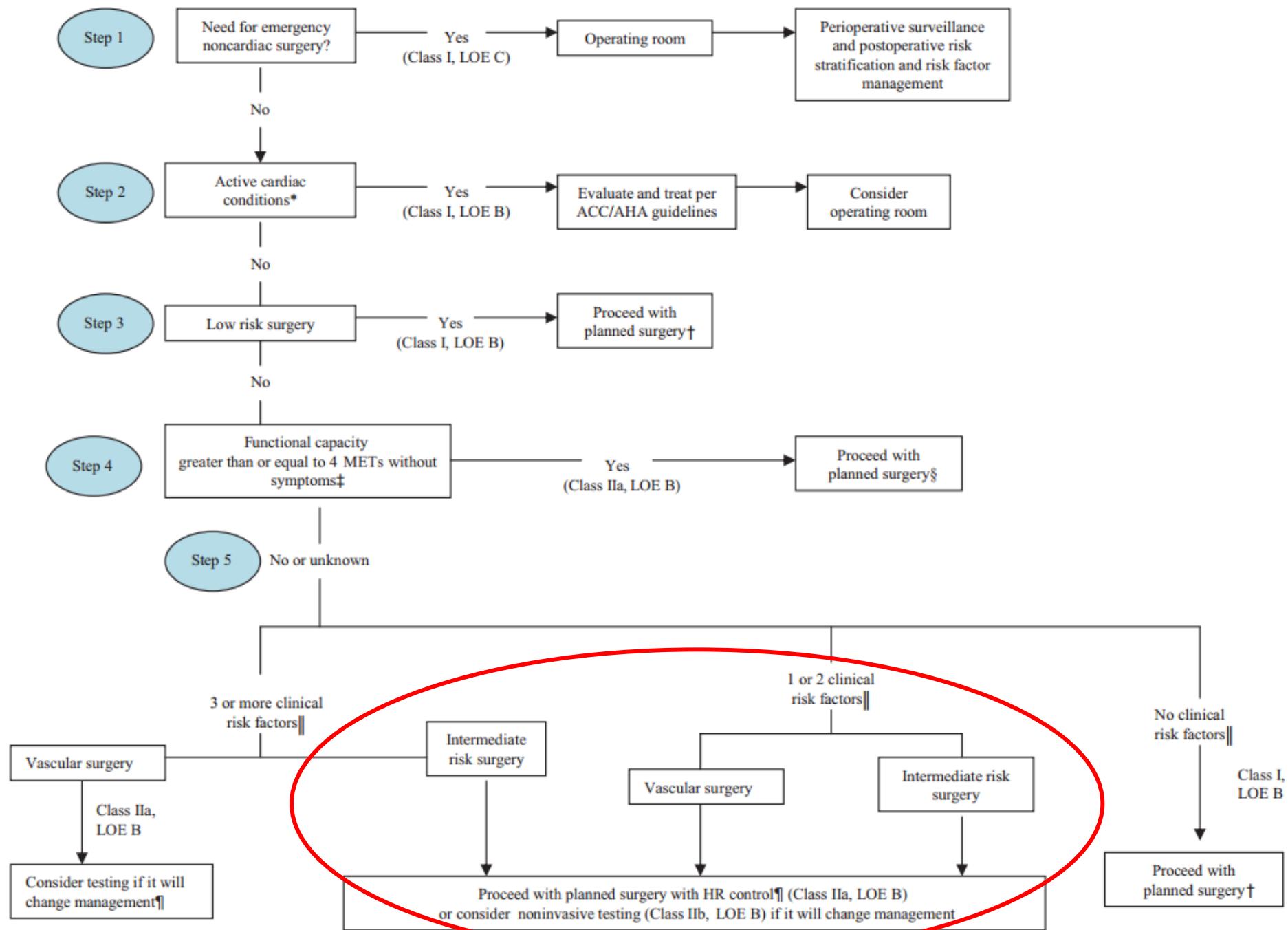


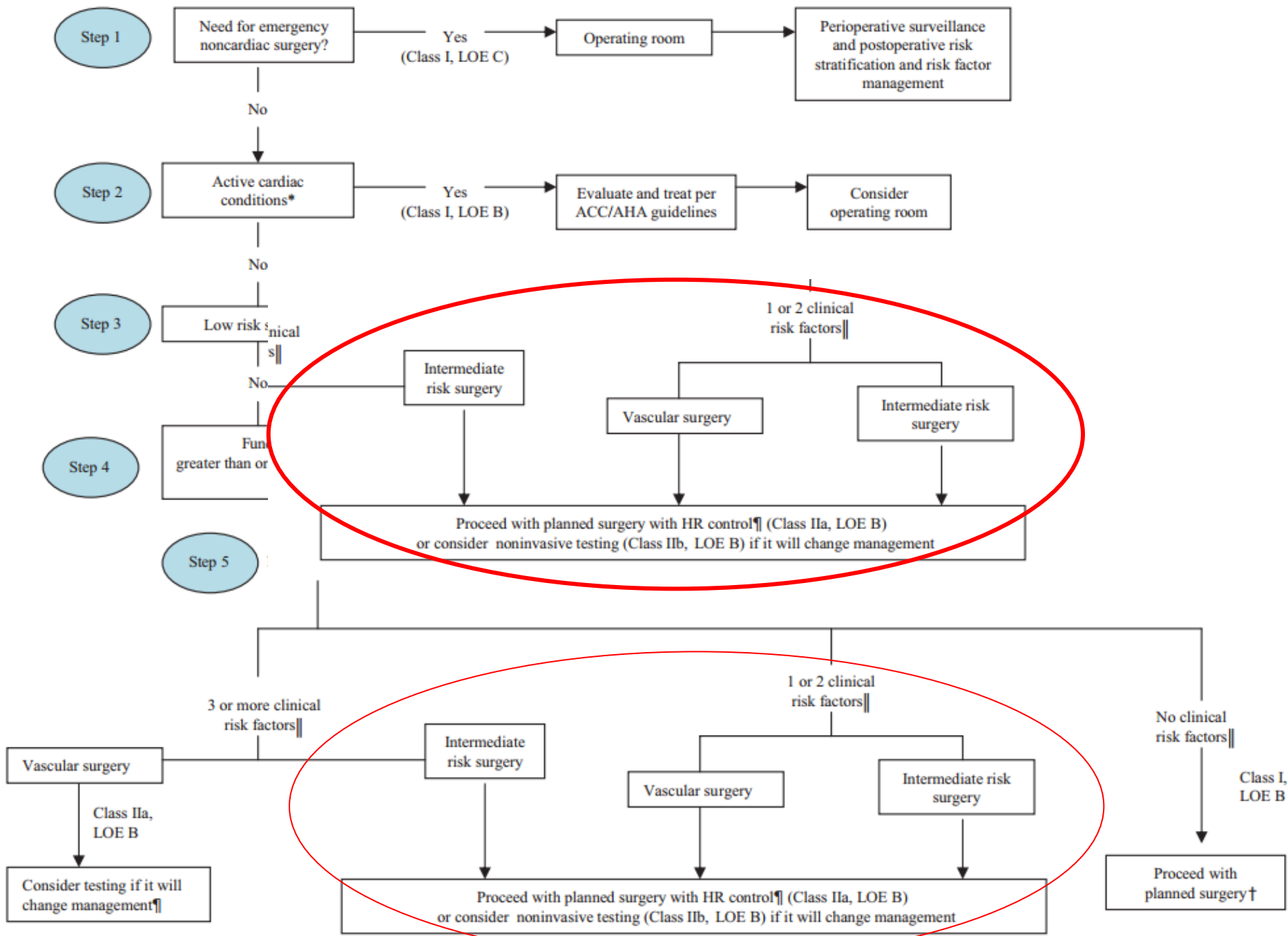












My recommendations

Preoperative coronary revascularization is still relevant in non-emergent surgery in patients with:

1. Active cardiac conditions.
2. Candidates for intermediate or high risk surgery in patients who have angina pectoris and important findings in non-invasive testing.*
3. Candidates for high-risk surgery in patients who have limited functional capacity (angina can not be excluded) and important findings in non-invasive testing.*

* Non-invasive testing is recommended

Thank you

Preoperative coronary revascularization is it still relevant?

Prof. Morris Mosseri

Head of Cardiology Division

Meir Medical Center, Kfar-Saba, Israel

8th International Conference

Acute Cardiac Care

Jerusalem, 18.6.2013

- אך יש להתייחס לקבוצות ספציפיות: גיל, חולים בסיכון גבוה, חולים עם ACS, סוג הניתוח

- האם טיפולים חדשניים שינו את המשוואה? DES מהדור החדש? נוגדי טסיות חדשים? ניתוח מעקפים עורקיים? בהיעדר עידכון הנחיות מידי חודש, שומה עלינו לעקוב מקרוב אחר הספרות המתחדשת ולכניס את הנתונים למשוואה.

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אולם יש להעיר הערה חשובה: כישלון המחקרים להוכיח שרווסקולריזציה כלילית לפני ניתוח (וגם ללא קשר לניתוח) מועילה יכול לנבוע מאחת משתי סיבות:

- טיפולים שמרניים מספיק טובים לייצוב העורקים ומניעת קרע של רובד טרשתי, ובמקביל ניהול חולה נכון במהלך הניתוח יכול למנוע צריכת חמצן מוגברת ואוטם מסוג 2 ולכן אין צורך בפעולות נוספות.
- הכישלון נובע מהעובדה שרווסקולריזציה כלילית כשלעצמה עדיין אינה פעולה מספיק בטוחה וכרוכה בסיבוכים במהלך הפעולה (המפרים את מאזן ה-risk-benefit לרעה), ובמיוחד כאשר מדובר ברווסקולריזציה ע"י CABG.
- אם ההסבר הוא השני, כי אז הנושא לא נסגר ואנו צריכים להמשיך ולחפש דרכים לרווסקולריזציה בטוחה יותר שתגן על החולים במהלך ניתוח לא-לבבי ולא תסכן אותם בעת ובעונה אחת.
- למשל: DES, פתיחת CTO בצנתור, ומאידך שיפור בטכניקות ניתוחיות.

- המסקנה מהנ"ל: יש להתאים את הטיפול ספציפית לכל חולה: Tailored or personalized medicine . צריך להתייחס להנחיות כאל הנחיות ולא כאל תורה למשה מסיני שאין לסטות ממנה.
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• התפתחות המחשבה בהערכת המדיניות להערכת חולים לקראת ניתוח לא לבבי

• אנמנזה

• איסוף נתונים רטרוספקטיביים על תוצאים של חולים שעברו ניתוחים לא-לבביים:

• RCT's of physiological tests + revascularization

• פער בין הנתונים הרטרוספקטיביים למחקרים הרנדומאליים (כשלון טיפול התערבותי למרות שמחלה כלילית הוכחה ככרוכה בעודף אירועים סביב לניתוח) יכול לנבוע מ:

– המבחנים הפיסיולוגיים שבוצעו לחולים לוקים בחסר (מבחנים כוזבים). יהיה נכון ב-LM ו-TVD.
(DECREASE).

• במקרה כזה, עקיפת המבחנים ובחינת הטיפול עצמו כמו במחקר של MONACO.

– הצלחת הטיפול הפרי-אופרטיבי בייצוב החולה ומניעת אירועים. במקרה כזה יש לצפות שלא יהיו סיבוכים פרי-אורטיביים, אולם יהיה שיפור לבבי בטווח הארוך. אולי זה במקרה בניסיון של הדסה.

– המחלה הכלילית של החולה קלה מידי ורווסקולריזציה אינה מועילה לטווח הקצר (הפרי-אופרטיבי) ולטווח הארוך (CARP).

– החסרונות המובנים של RCT's (קבוצה קטנה ונבחרת מכלל האוכלוסייה, DECREASE ו-CARP).

– הטיפול ההתערבותי כרוך בעצמו בסיכון והתועלת בו קטנה כשלעצמה או שהסיכון אינו שווה את התועלת שהפעולה משיגה (יהיה נכון בעיקר בחולים קשים שבהם רווסקולריזציה כבר עינה יכולה להועיל או שהיא מסוכנת מידי) (DECREASE).

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• ובינתיים כיצד להתגבר על החסרונות?