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Perioperative Medication Management in the Rheumatic Disease

Perioperative Medication Management in the Rheumatic Disease

OBJECTIVES

Preoperative assessment of patients with rheumatic diseases:

- Optimizing the medication regimen (DMARDS, Biologics)
- Preoperative steroid stress dose
- Anticoagulation
- Cardiovascular risk stratification



Perioperative Medication Management in the Rheumatic Disease

Complexity

- Coexisting illness, multiple organ involvement
- Increased risk of thrombosis
- High postoperative mortality/morbidity
- knowledge of and recommendations
- Guidelines by professional bodies



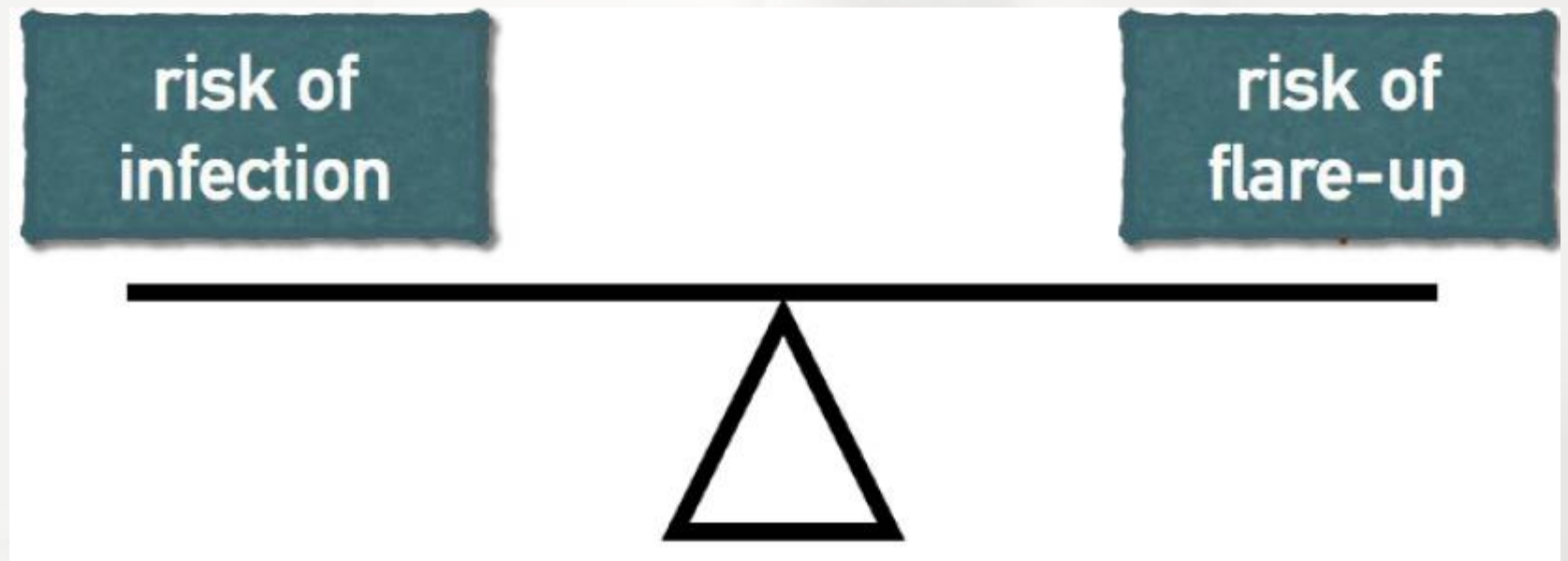
Perioperative Medication Management in the Rheumatic Disease

Wether DMARDs should be discontinued?

- No defined standard of perioperative care
- Risk/benefit analysis
 - Infection and wound healing complications
 - Disease activity



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SPECIAL ARTICLE

2017 American College of Rheumatology/ American Association of Hip and Knee Surgeons Guideline for the Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty

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DMARDs, (elective THA or TKA in RA, SPA, GIA, SLE)

Continue the current dose of:

- Methotrexate
- Leflunomide
- Hydroxychloroquine
- Sulfasalazine
- No increase risk of infections
- Disease flares after surgery occur frequently

GOODMAN SM et al. Arthritis Care & Research 2017; 69:1111–24

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DMARDs, (THA or TKA in severe SLE)

Continue current dose of:

- Mycophenolate mofetil
- Azathioprine
- Cyclosporine
- Tacrolimus
- For elective THA or TKA



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DMARDs (THA or TKA in non severe SLE)

Withhold current dose of: (1wk prior to surgery)

- Mycophenolate mofetil
- Azathioprine
- Cyclosporine
- Tacrolimus
- Restarted at 3–5 days





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Biologic agents

- Withhold all biologic agents in elective THA or TKA
- Plan the surgery at the end of the dosing cycle for that medication
- ?Serum half-life

- GOODMAN SM et al. Arthritis Care & Research 2017; 69:1111–24
- Dutch Society for Rheumatology. Medicines [online], www.nvr.nl (2003)
- Ledingham J. et al. Rheumatology (Oxford) 2005; 44:157–163

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Biologic agents

- Restart with the evidence of wound healing
- All sutures/staples are out
- No swelling, erythema, or drainage
- No evidence of non-surgical site infections
- 14 days



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Prednisolone stress dose

- Fear of adrenal gland insufficiency
- ACTH stimulation
- 'stress dose' **only** for patients with abnormal cosyntropin test?

Bissar L,et al. Open Rheumatology Journal 2013; 7:42-50



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Do not need stress dose of steroid:

- Any patient who has been taking any dose of glucocorticoid for < 3 weeks
- Patients on morning doses of < 5 mg/day of prednisolone any length of time
- Patients on < 10 mg of prednisolone every other day



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Need stress dose of steroid:

- Any patient on >20 mg/day of prednisolone for > 3 weeks
- Any patient on glucocorticoids with clinical Cushing's syndrome



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Intermediate group (unknown HPA status):

- Patients on 5 to 20 mg of prednisolone >3 WK
- 5 mg of prednisolone daily in **evening**
- ≥ 3 intraarticular, 3 months prior to surgery





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Steroid Stress dose:

- The high infection rate,(compared with most conventional DMARDs and biologics)
 - ACTH stimulation?
-
- MacKenzie CR. Curr Rev Musculoskelet Med 2017; 10:404–6
 - MacKenzie CR, Goodman SM. Curr Rheumatol Rep 2016; 18:47
 - GOODMAN SM et al. Arthritis Care & Research 2017; 69:1111–24



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- Continue the current dose of glucocorticoids
- No need to start “stress dosing”
- Prednisone ≤ 16 mg/day
- Cut-off for immunosuppression at 20 mg of prednisone/day for at least 2 weeks
- Tapering steroid prior to surgery to ,20 mg/day

GOODMAN SM et al. Arthritis Care & Research 2017; 69:1111–24

Goodman SM, Bass AR. BMC Rheumatology 2018; 2:2

Gualtierotti RG et al. Adv Ther 2018; 35:439–56

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Management of hypercoagulable state:

- At risk of both thrombosis & bleeding
- Hypercoagulability despite warfarin or heparin therapy
- Surgical stress → **catastrophic** APS

APS is classified in the **very high risk** category for venous thromboembolism during the postoperative period

Gualtierotti RG et al. Adv Ther 2018; 35:439–56



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Risk of Thromboembolism:

- Mechanical heart valve
- Atrial fibrillation
- VTE
- Active cancer
- Recent stroke
- Diabetes
- Significant thrombophilia
- Age > 75
- CHF
- Hypertension



Risk stratification

High risk

- VTE
- Atrial fibrillation
- Mechanical heart valve
- Severe thrombophilia (APS)

Moderate risk

- Bileaflet aortic valve prosthesis plus at least one of the following: Atrial fibrillation, prior CVA/TIA, hypertension, diabetes mellitus, CHF or age >75 years
- Atrial fibrillation with CHADS₂ score 3 or 4
- VTE within previous 3–12 months, recurrent VTE, non-severe thrombophilia or active cancer

Low risk

- Bileaflet aortic valve without atrial fibrillation or stroke risk factors
- CHADS₂ score 0–2
- Single VTE >12 months ago and no other risk factors

Recommended bridging anticoagulation therapy

- Stop warfarin 5 days ahead of surgery
- Start therapeutic-dose subcutaneous LMWH or intravenous UFH
- Stop LMWH and UFH 24 h and 4 h before surgery, respectively
- Check INR on the morning of surgery
- (Grade 1C)

- Bridging anticoagulation with therapeutic-dose or low-dose subcutaneous LMWH or therapeutic-dose intravenous UFH preferred over no bridging during temporary interruption of warfarin therapy
- (Grade 2C)

- Bridging anticoagulation with low-dose subcutaneous LMWH or no bridging preferred over bridging with therapeutic-dose subcutaneous LMWH or intravenous UFH
- (Grade 2C)

Bridging Therapy

-5 days	Discontinue warfarin
-3 days	Check INR and Kidney Function Start therapeutic dose LMWH (e.g., enoxaparin 1 mg/kg BID or 1.5 mg/kg QD) Adjust LMWH dose on the basis of creatinine clearance
-24 hours	Administer the last dose of LMWH 24 h before surgery (50 % of the dose for once-daily regimens)
Day 0	Schedule for early morning surgery Check INR if needed If INR is still elevated ($\text{INR} \geq 1.5$), consider low-dose (1–2 mg) oral vitamin K Use aggressive perioperative mechanical DVT prophylaxis Start warfarin in the evening (regular dose)
+24 hours	Start prophylactic or therapeutic dose LMWH (can be delayed for 48–72 hours for patients undergoing high bleeding risk surgery)
+4–5 days	Discontinue LMWH when INR is therapeutic





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Preparing APS patients for surgery(anticoagulated)

- Risk of bleeding/thromboembolism
- Absence of study data that address the issue of perioperative anticoagulation management

- American College of Chest Physicians (ACCP) 2014
- UK National Institute for Health and Clinical Excellence (NICE) guidelines for reducing the risk of thromboembolism

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- The “second-hit hypothesis”
- Risk of vascular events in aPL-positive patients increases with number of thrombosis risk factors

SaundersKH, ErkanD. Perioperativemanagement ofantiphospholipid antibody positive patients during non-cardiac surgeries. In: Mandell BF, editor. Perioperative management of the patient with rheumatic disease. 1st ed. New York: Springer; 2012. p. 91–107



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- “Clinically significant” aPL profile → risk for perioperative thrombosis
- ? studies for accurate dosing
- Current recommended doses result in “under-anticoagulation”
- Risk of perioperative bleeding



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Table 2. Recommendations⁷ of standard antithrombotic regimens to prevent venous thromboembolism in high risk general and orthopedic surgery patients. These dosing schedules may result in “under-anticoagulation” of APS patients and should be the minimum administered dose.

Surgery	LDU Heparin	LMW Heparin*
General surgery	5,000 U q 8–12 h, start 1–2 h before surgery	30 mg q 12 h, start 8–12 h after surgery or 40 mg q 24 h, start 1–2 h before surgery
Orthopedic surgery	5,000 U q 8–12 h, start 12–24 h after surgery	30 mg q 12 h, start 12–24 h after surgery or 40 mg q 24 h, start 10–12 h before surgery

LDU: low dose unfractionated; LMW: low molecular weight.

*Dosing schedule for enoxaparin (other LMW heparin preparations available for perioperative thrombosis prophylaxis are ardeparin, dalteparin, danaparoid, nadroparin, and tinzaparin). These LMW preparations have similar clinical efficacy and the choice of medication depends on physician preference^{44,45}.



Erkan D et al. J Rheumatol 2002;29:843-49
William HG. et al. CHEST 2001; 119:132S–175S

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- Prophylaxis for (nonAPS) stable rheumatic disease
- Patients with active disease are considered as **high risk** for VTE



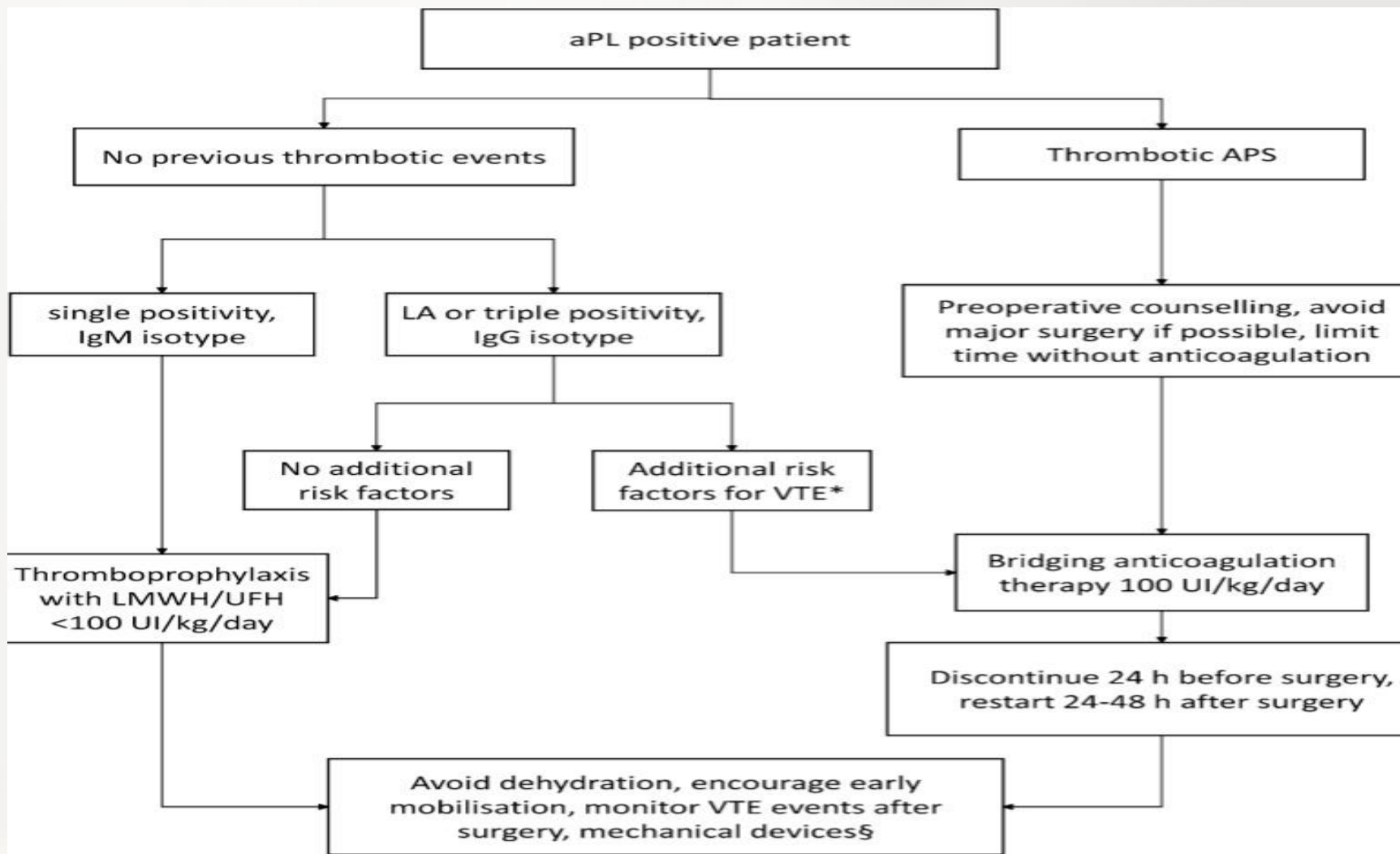


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Risk of cardiovascular disease:

- Continue aspirin, if already in treatment (sec. prophylaxis)
- Beta-blockers
- Hydroxychloroquine
- Statins
- Risk assessment for cardiovascular disease and thrombosis

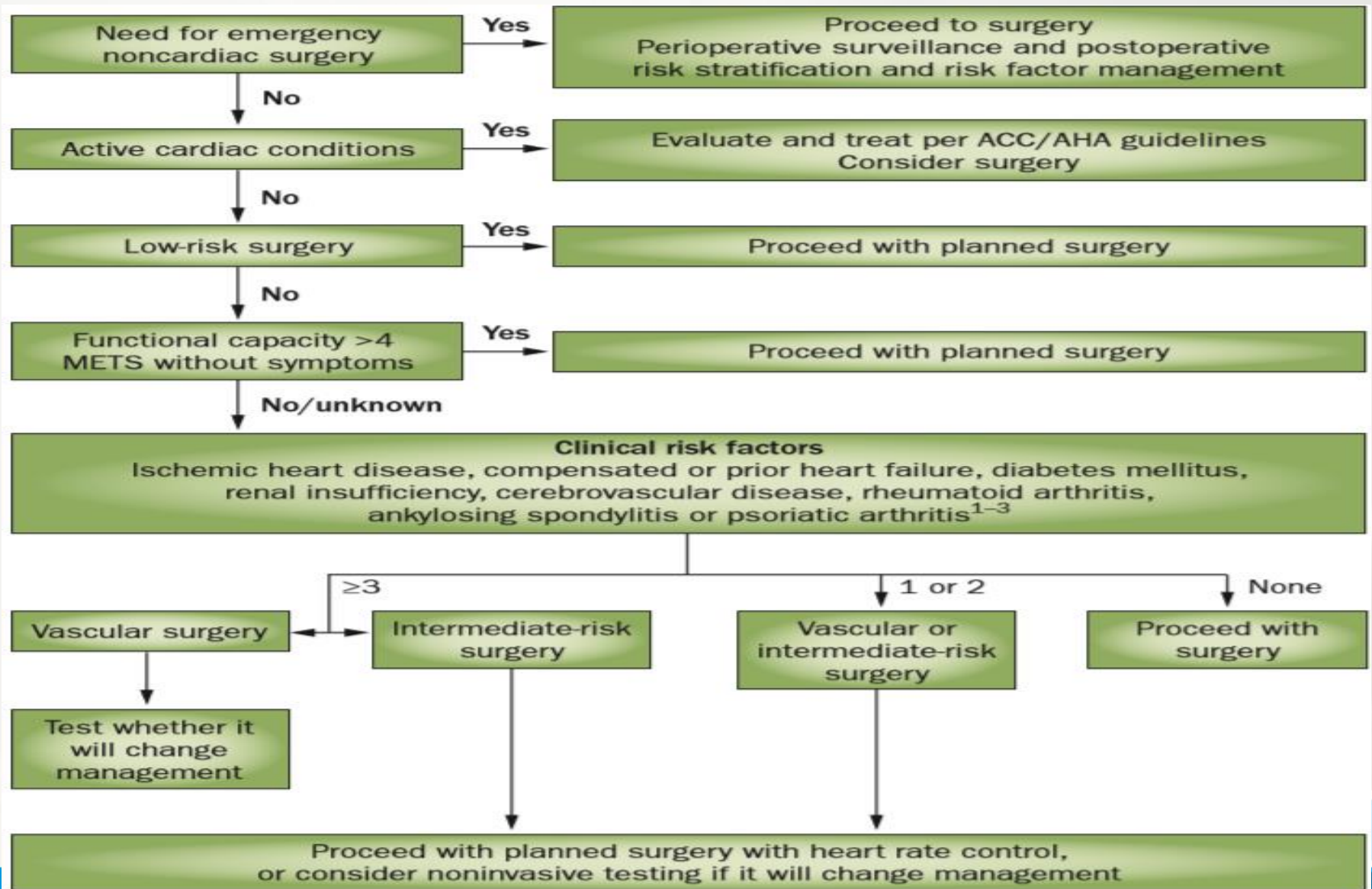
Gualtierotti RG et al. Adv Ther 2018; 35:439–56



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- Increased risk of cardiovascular related death
- Non explainable with traditional risk
- Fewer symptoms of angina





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Low risk procedures for cardiac disease:

- Ophthalmologic procedures
- Superficial dermatologic procedures
- Cataract surgery
- Breast surgery
- Endoscopy



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Perioperative Antibiotic Prophylaxis:

- Current guidelines for the prevention of surgical infections
- The optimal timing and duration of prophylaxis is controversial
- Prophylactic antibiotics within 60 min before skin incision and stopping it within 24 h postoperatively



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Editor

Perioperative Management of Patients with Rheumatic Disease

 Springer

