**Review Article : NEW TRENDS IN THE ANAESTHETC MANAGEMENT OF ADULT PATIENTS WITH MYOCARDIAL ISCHEMIA DURING NON CARDIAC SURGRY**

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**Abstract**

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| Cardiac *i*patients *i*undergoing *i*non-cardiac *i*surgery *i*require *i*thorough *i*preoperative *i*assessment. *i*Several *i*systems *i*have *i*been *i*developed *i*to *i*evaluate *i*patients' *i*general *i*and *i*cardiac *i*conditions. *i*Administering *i*anesthesia *i*to *i*patients *i*with *i*preexisting *i*cardiac *i*disease *i*is *i*an *i*interesting *i*challenge. *i*There *i*is *i*no *i*standard *i*rule *i*for *i*anesthetic *i*management *i*of *i*cardiac *i*patients; *i*management *i*is *i*tailored *i*according *i*to *i*the *i*patient's *i*condition *i*and *i*the *i*nature *i*of *i*the *i*cardiac *i*disease *i*as *i*well *i*as *i*the *i*type *i*and *i*risk *i*of *i*planned *i*surgery. *i*Cardiac *i*complications *i*after *i*non-cardiac *i*surgery *i*depend *i*not *i*only *i*on *i*patient *i*specific *i*risk *i*factors *i*but *i*also *i*on *i*the *i*type *i*of *i*surgery *i*and *i*the *i*circumstances *i*under *i*which *i*it *i*takes *i*place *i*and *i*anesthetic *i*management. *i*Postoperative *i*Surveillance *i*and *i*Pain *i*Management *i*play *i*a *i*major *i*role *i*in *i*improving *i*the *i*perioperative *i*outcomes *i*and *i*must *i*be *i*included *i*in *i*the *i*perioperative *i*plan. *i*Future *i*research *i*should *i*be *i*directed *i*at *i*determining *i*the *i*value *i*of *i*prophylactic *i*medical *i*therapy *i*versus *i*more *i*extensive *i*diagnostic *i*testing *i*and *i*interventions.  **Keywords**  anaesthetic *i*mangment; *i*cardiac *i*complictions; *i*cardiac *i*patients; *i*non *i*cardiac *i*surgery; *i*risk *i*factors. |

**1.Introduction**

Cardiac *i*diseases *i*particularly *i*ischemic *i*is *i*the *i*medical *i*illnesses *i*most *i*frequently *i*encountered *i*in *i*anesthetic *i*practice, *i*and *i*a *i*major *i*cause *i*of *i*perioperative *i*morbidity *i*and *i*mortality1***.***More *i*than *i*one *i*half *i*of *i*postoperative *i*deaths *i*are *i*caused *i*by *i*cardiac *i*events, *i*most *i*of *i*which *i*are *i*ischemic *i*in *i*origin2 *i****.***One *i*of *i*the *i*biggest *i*challenges *i*for *i*anaesthetists *i*today *i*is *i*the *i*safe *i*conduct *i*of *i*anaesthesia *i*for *i*patients *i*who *i*might *i*be *i*elderly, *i*have *i*preexisting *i*documented *i*or *i*asymptomatic *i*cardiac *i*disease *i*and *i*are *i*scheduled *i*to *i*undergo *i*non-cardiac *i*surgery3***. i***The *i*perioperative *i*management *i*of *i*a *i*patient *i*with *i*cardiovascular *i*disease *i*requires *i*close *i*cooperation *i*between *i*the *i*cardiologist, *i*surgeon, *i*and *i*anesthesiologist***4.***The *i*European *i*Society *i*of *i*Cardiology(ESC) *i*and *i*the *i*European *i*Society *i*of *i*Anaesthesiology *i*(ESA) *i*Guidelines *i*recommend *i*a *i*practical, *i*stepwise *i i*evaluation *i*not *i*to *i*“get *i*medical *i*clearance” *i*but *i*rather *i*to *i*evaluate *i*the *i*patient’s *i*medical *i*status *i*and *i*integrates *i*clinical *i*risk *i*factors *i*and *i*test *i*results *i*with *i*the *i*estimated *i*stress *i*of *i*the *i*planned *i*surgical *i*procedure. *i*This *i*results *i*in *i*an *i*individualized *i*cardiac *i*risk *i*assessment, *i*with *i*the *i*opportunity *i*of *i*initiating *i*medical *i*therapy, *i*coronary *i*interventions, *i*and *i*specific *i*surgical *i*and *i*anaesthetic *i*techniques *i*in *i*order *i*to *i*optimize *i*the *i*patient’s *i*perioperative *i*condition4.Surgery *i*, *i*with *i*its *i*associated *i*trauma *i*, *i*anesthesia *i*and *i*analgesia *i*, *i*intubation *i*and *i*extubation, *i*pain, *i*hypothermia, *i*bleeding *i*and *i*anaemia, *i*and *i*fasting *i*are *i*factors *i*that *i*ini­tiate *i*inflammatory, *i*hypercoagulable, *i*stress *i*and *i*hypoxic *i*state, *i*which *i*is *i*associated *i*with *i*perioperative *i*elevations *i*in *i*troponin *i i*levels,arterial *i*thrombosis *i*and *i*mortality5 *i*.Tachycardia *i*and *i*hypertension, *i*common *i*in *i*the *i*perioperative *i*period, *i*may *i*exert *i*excess *i*shear *i*forces *i*on *i*vulnerable *i*plaques *i*with *i*thin *i*fibrous *i*caps *i*and *i*high *i*circumferential *i*tensile *i*stress *i*or *i*cause *i*endothelial *i*stripping *i*or *i*erosion *i*of *i*plaques *i*with *i*severe *i*coronary *i*stenosis, *i*associated *i*with *i*high *i*blood *i*velocities**6**

**2.Review**

Risk *i*stratifcation *i*of *i*patients *i*with *i*known, *i*or *i*at *i*risk *i*of *i*coronary *i*artery *i*disease *i*is *i*usually *i*based *i*on**:(1)** *i*Assessment *i*of *i*clinical *i*risk *i*factors *i*of *i*the *i*patient *i*which *i*can *i*be *i*obtained *i*by *i i*history *i*,clinical *i*examination *i*and *i*investigations *i i*to *i*assess *i*the *i*cardiac *i*risk**.(2)** *i*Assessment *i*of *i*the *i*surgical *i*risk *i*for *i*cardiac *i*events**.(3)** *i*Risk *i*stratification *i*by *i i*multivariate *i*cardiac *i i*risk *i*indecies *i*to *i*create *i*a *i*stepwise *i*approach *i i*for *i*perioprative *i i*assessment *i*of *i*the *i*patient7 *i i*.

***Step iwise iapproach iof i2014 iAmerican iCollege iof iCardiology i/American iHeart iAssociation iguidelines iof ipreoperative iassessment iof imyocardial iischemic ipatient ifor inon icardiac isurgery7:***

***Step i1***:

In *i*patients *i*scheduled *i*for *i*surgery *i*with *i*risk *i*factors *i*for *i*or *i*known *i*coronary *i*artery *i*disease, *i*determine *i*theurgency *i*of *i*surgery. *i*If *i*an *i*emergency, *i*then *i*determine *i*the *i*clinical *i*risk *i*factors *i*that *i*may *i*influence *i*perioperative *i*management *i*and *i*proceed *i*to *i*surgery *i*with *i*appropriate *i*monitoring *i*and *i*management *i*strategies *i*based *i*on *i*the *i*clinical *i*assessment.

***Step i2:***

If *i*the *i*surgery *i*is *i*urgent *i*or *i*elective, *i*determine *i*if *i*the *i*patient *i*has *i*an *i*acute *i*coronary *i*syndrome. *i*If *i*yes, *i*then *i*refer *i*patient *i*for *i*cardiology *i*evaluation *i*and *i*management. *i*

***Step i3:***

If *i*the *i*patient *i*has *i*risk *i*factors *i*for *i*stable *i*coronary *i*disaese, *i*then *i*estimate *i*the *i*perioperative *i*risk *i*of *i*major *i*adverse *i*cardiac *i*events *i*(MACE) *i*on *i*the *i*basis *i*of *i*the *i*combined *i*clinical/surgical *i*risk. *i*

***Step i4***

If *i*the *i*patient *i*has *i*a *i*low *i*risk *i*of *i*major *i*adverse *i*cardiac *i*events *i*(<1%), *i*then *i*no *i*further *i*testing *i*is *i*needed, *i*and *i*the *i*patient *i*may *i*proceed *i*to *i*surgery. *i*

***Step i5:***

If *i*the *i*patient *i*is *i*at *i*elevated *i*risk *i*of *i*of *i*major *i*adverse *i*cardiac *i*events, *i*then *i*determine *i*functional *i*capacity *i*with *i*an *i*objective *i*measure *i*. *i*If *i*the *i*patient *i*has *i*moderate, *i*good, *i*or *i*excellent *i*functional *i*capacity *i*(>4 *i*METs), *i*then *i*proceed *i*to *i*surgery *i*without *i*further *i*evaluation. *i*

***Step i6:***

If *i*the *i*patient *i*has *i*poor *i*(<4 *i*METs) *i*or *i*unknown *i*functional *i*capacity, *i*then *i*the *i*clinician *i*should *i*consult *i*with *i*the *i*patient *i*and *i*perioperative *i*team *i*to *i*determine *i*whether *i*further *i*testing *i*will *i*impact *i*patient *i*decision *i*making *i*(e.g., *i*decision *i*toperform *i*original *i*surgery *i*or *i*willingness *i*to *i*undergo *i*Percutaneus *i*coronary *i*Intervention(PCI) *i*or *i i*Coronary *i*Artery *i*Bypass *i*Graft(CABG), *i*depending *i*on *i*the *i*results *i*of *i*the *i*test) *i*or *i*perioperative *i*care. *i*If *i*yes, *i*then *i*pharmacological *i*stress *i*testing *i*is *i*appropriate. *i*In *i*those *i*patients *i*with *i*unknown *i*functional *i*capacity, *i*exercise *i*stress *i*testing *i*may *i*be *i*reasonable *i*to *i*perform. *i*If *i*the *i*stress *i*testis *i*abnormal, *i*consider *i*coronary *i*angiography *i*and *i*revascularization *i*depending *i*on *i*the *i*extent *i*of *i*the *i*abnormal *i*test. *i*The *i*patient *i*can *i*then *i*proceed *i*to *i*surgery *i*with *i i*guide *i*line *i*directed *i*medical *i*therpy *i*or *i*consider *i*alternative *i*strategies, *i*such *i*as *i*noninvasive *i*treatment *i*of *i*the *i*indication *i*for *i*surgery *i*(e.g., *i*radiation *i*therapy *i*for *i*cancer) *i*or *i*palliation. *i*If *i*the *i*test *i*is *i*normal,proceed *i*to *i*surgery *i*according *i*to *i*guide *i*line *i*directed *i*medical *i*therpy.

***Step i7:***

If *i*testing *i*will *i*not *i*impact *i*decision *i*making *i*or *i*care, *i*then *i*proceed *i*to *i*surgery *i*according *i*to *i*guide *i*line *i*directed *i*medical *i*therpy *i*or *i*consider *i*alternative *i*strategies, *i*such *i*as *i*noninvasive *i*treatment *i*of *i*the *i*indication *i*for *i*surgery7.

***(1) iAssessment iof iclinical irisk ifactors:***

**I)**Determination *i*of *i*functional *i*capacity *i*which *i*is *i*a *i*pivotal *i*step *i*in *i*pre-operative *i*cardiac *i*risk *i*assessment *i*and *i*is *i*measured *i*in *i*metabolic *i*equivalents *i*(METs). *i*One *i*MET *i*equals *i*the *i*basal *i*metabolic *i*rate. *i i*1 *i*MET *i*is *i*defined *i*as *i*3.5 *i*mL *i*O2 *i*uptake/kg *i*per *i*min, *i*which *i*is *i*the *i*resting *i*oxygen *i*uptake *i*in *i*a *i*sitting *i*position. *i*Exercise *i*testing *i*provides *i*an *i*objective *i*assessment *i*of *i*functional *i*capacity. *i*Without *i*testing, *i*functional *i*capacity *i*can *i*be *i*estimated *i*from *i*the *i*ability *i*to *i*perform *i*the *i*activities *i*of *i*daily *i*living. *i*One *i*MET *i*represents *i*metabolic *i*demand *i*at *i*rest; *i*climbing *i*two *i*flights *i*of *i*stairs *i*demands *i*4 *i*METs, *i*and *i*strenuous *i*sports, *i*such *i*as *i*swimming,.10 *i*METS8 *i.*The *i*inability *i*to *i*climb *i*two *i*flights *i*of *i*stairs *i*or *i*run *i*short *i*distance *i*(<4 *i*METs) *i*indicates *i*poor *i*functional *i*capacity *i*associated *i*with *i*an *i*increased *i*incidence *i*of *i*post-operative *i*cardiac *i*events9 *i****.***Another *i*method *i*of *i*classifying *i*functional *i*capacity *i*for *i*those *i*patients *i*with *i*known *i*cardiac *i*disease *i*is *i*the *i*New *i*York *i*Heart *i*Association *i*(NYHA) *i*classification *i*as *i*shown *i*in *i*table(1 *i*)10 *i*.

|  |  |
| --- | --- |
| **Class** | **Description** |
| **I** | Patients *i*with *i*cardiac *i*disease *i*but *i*without *i*resulting *i*limitation *i*of *i*physical *i*activity *i*due *i*to *i*fatigue, *i*palpitations, *i*dyspnea *i*or *i*angina. |
| **II** | Patients *i*with *i*cardiac *i*disease *i*resulting *i*in *i*slight *i*limitation *i*in *i*physical *i*activity. |
| **III** | Patients *i*with *i*marked *i*limitation *i*of *i*physical *i*activity. |
| **IV** | Patients *i*with *i*cardiac *i*disease *i*who *i*are *i*unable *i*to *i*carry *i*out *i*any *i*physical *i*activity *i*without *i*discomfort. *i*Symptoms *i*of *i*angina *i*or *i*heart *i*failure *i*may *i*be *i*present *i*at *i*rest. |

Table(1 *i*) *i i*after *i****(American iHeart iAssociation, i1994).***

**II)**Investigations *i*:Preoprative *i*investigations *i*include *i*resting *i*ECG, *i*biomarkers, *i*restingechocardiography, *i*stress *i*testing *i*and *i*invasive *i*coronary *i*angiography.

**A)Resting *i*12 *i*-Lead *i*ECG *i*:**The *i*pre-operative *i*ECG *i*offers *i*important *i*prognostic *i*information *i*and *i*is *i*predictive *i*of *i*long-term *i*outcome, *i*independent *i*of *i*clinical *i*findings *i*and *i i*perioperative *i*ischaemia. *i*However, *i*the *i*ECG *i*may *i*be *i*normal *i*or *i*non-specific *i*in *i*patients *i*with *i*myocardial *i*ischaemia *i*or *i*even *i*with *i*infarction11***. i***The *i*resting *i*ECG *i*may *i*show *i*signs *i*of *i*coronary *i*artery *i*disease *i*such *i*as *i*previous *i*myocardial *i*infarction *i*or *i*an *i*abnormal *i*repolarization *i*pattern. *i*The *i*ECG *i*may *i*assist *i*in *i*clarifying *i*the *i*differential *i*diagnosis *i*if *i*taken *i*in *i*the *i*presence *i*of *i*pain, *i*allowing *i*detection *i*of *i*dynamic *i*ST-segment *i*changes *i*like *i*ST-segment *i*depression *i*or *i*transient *i*elevation *i*and/or *i*T-wave *i*changes *i*which *i*is *i*characteristic *i*ECG *i*abnormalties *i*in *i*non *i*ST- *i*segment *i*elevation *i*acute *i*coronary *i*syndrome, *i*non *i*ST- *i*segment *i*elevation *i i*acute *i*coronary *i*syndrome. *i*The *i*ECG *i*may *i*also *i*show *i*other *i*abnormalities *i*such *i*as *i*left *i*ventricular *i*hypertrophy *i*(LVH), *i*bundle *i*branch *i*block, *i*pre-excitation, *i*arrhythmias, *i*or *i*conduction *i*defects12 *i****.***

**B) *i*Biomarkers *i*:**Cardiac *i*troponins *i*play *i*a *i*central *i*role *i*in *i*establishing *i*a *i*diagnosis *i*and *i*stratifying *i*risk, *i*and *i*make *i*it *i*possible *i*to *i*distinguish *i*between *i*non *i*ST-segment *i*elevation *i*myocardial *i*infarction *i*and *i*unstable *i*angina. *i*Troponins *i*are *i*more *i*specific *i*and *i*sensitive *i*than *i*the *i*traditional *i*cardiac *i*enzymes *i*such *i*as *i*creatine *i*kinase *i*(CK), *i*its *i*isoenzyme *i*MB *i*(CK-MB), *i*and *i*myoglobin. *i*Elevation *i*of *i*cardiac *i*troponins *i*reflects *i*myocardial *i*cellular *i*damage, *i*which *i*in *i*non *i*ST-segment *i*elevation *i*acute *i*coronary *i*syndrome *i*may *i*result *i*from *i*distal *i*embolization *i*of *i*platelet-rich *i*thrombi *i*from *i*the *i*site *i*of *i*a *i*ruptured *i*or *i*eroded *i*plaque. *i*Accordingly, *i*troponin *i*may *i*be *i*seen *i*as *i*a *i*surrogate *i*marker *i*of *i*active *i*thrombus *i*formation. *i*In *i*the *i*setting *i*of *i*myocardial *i*ischaemia *i*(chest *i*pain, *i*ECG *i*changes, *i*or *i*new *i*wall *i*motion *i*abnormalities), *i*troponin *i*elevation *i*indicates *i*myocardial *i*infarction. *i*In *i*patients *i*with *i*myocardial *i*infarction, *i*an *i*initial *i*rise *i*in *i*troponins *i*occurs *i*within *i*4 *i*h *i*after *i*symptom *i*onset. *i*Troponins *i*may *i*remain *i*elevated *i*for *i*up *i*to *i*2 *i*weeks *i*due *i*to *i*proteolysis *i*of *i*the *i*contractile *i*apparatus. *i*In *i*non *i*ST- *i*segment *i i*elevation *i*acute *i*coronary *i*syndrome, *i*minor *i*troponin *i*elevations *i*usually *i*resolve *i*within *i*48 *i*– *i*72h13.

Possible *i i*non-acute *i*coronary *i*syndrome *i*causes *i*of *i*troponin *i*elevation *i*(important *i*differential *i*diagnoses):

• *i*Chronic *i*or *i*acute *i*renal *i*dysfunction *i i*

• *i*Pulmonary *i*embolism, *i*severe *i*pulmonary *i*hypertension.

• *i*Aortic *i*dissection, *i*aortic *i*valve *i*disease *i*or *i*hypertrophic *i i*cardiomyopathy

• *i*Hypothyroidism

• *i*Burns, *i*if *i*affecting *i*>30% *i*of *i*body *i*surface *i*area

• *i*Rhabdomyolysis.

• *i*Critically *i*ill *i*patients, *i*especially *i*with *i*respiratory *i*failure, *i*or *i*sepsis13***.***In *i*the *i*perioperative *i*setting, *i*assessment *i*of *i*cardiac *i*troponins *i*in *i*high-risk *i*patients, *i*both *i*before *i*and *i*48– *i*72 *i*hours *i*after *i*major *i*surgery, *i*may *i*therefore *i*be *i*considered14*.****.***Existing *i*evidence *i*suggests *i*that *i*even *i*small *i*increases *i*in *i*cardiac *i*tropinin *i*-T *i*in *i*the *i*perioperative *i*period *i*reflect *i*clinically *i*relevant *i*myocardial *i*injury *i*with *i*worsened *i*cardiac *i*prognosis *i*and *i*outcome15***.***During *i*noncardiac *i*surgery, *i*the *i*peak *i*postoperative *i*tropinin *i*-T *i*measurement *i*during *i*the *i*first *i*3 *i*days *i*after *i*surgery *i*was *i*significantly *i*associated *i*with *i*30-day *i*mortality. *i*Monitoring *i i*postoperative *i*TnT *i*measurements *i*can *i*enhance *i*risk *i*stratification *i*after *i*non *i*cardiac *i*surgery14***.***Another *i*important *i*biomarkers *i*are *i*B-type *i*natriuretic *i*peptide *i*(BNP) *i*and *i*N-terminal *i*pro-BNP(NT-proBNP) *i*are *i*produced *i*in *i*cardiac *i*myocytes *i*in *i*response *i*to *i*increases *i*in *i*myocardial *i*wall *i*stress16. *i*Pre-operative *i*measurement *i*of *i*BNP *i*or *i*NT- *i*proBNP *i*was *i*recommended *i*to *i*obtain *i*prog-nostic *i*information *i*on *i*perioperative *i*and *i*late *i*cardiac *i*events *i*in *i*high-risk *i*patients17**.**

**(C) *i*Resting *i*Echocardiography: *i***Transthoracic *i*echocardiography *i*allows *i*rapid, *i*non-invasive, *i*point-of-care *i*assessment *i*of *i*ventricular *i*function, *i*valvular *i*integrity, *i*volume *i*status *i*and *i*fluid *i*responsiveness. *i*It *i*can *i*help *i*distinguish *i*undifferentiated *i*systolic *i*murmurs *i*preoperatively, *i*give *i*valuable *i*information *i*on *i*the *i*aetiology *i*of *i*unexplained *i*hypotension *i*and *i*cardiovascular *i*collapse *i*and *i*assess *i*response *i*to *i*therapeutic *i*interventions *i*such *i*as *i*vasoactive *i*drugs *i*and *i*volume *i*resuscitation18*.*Left *i*ventricular *i*ejection *i*fraction(Ef) *i*and *i*fractional *i*shortening(FS) *i*are *i i*used *i*for *i i*systolic *i*function *i*assessment. *i*Normal *i*range *i*of *i*EF *i*is *i i*55 *i*to *i*70***%17.***Appropriate *i*perioperative *i*indications *i*of *i*echocardiography *i*include *i*(but *i*are *i*not *i*limited *i*) *i*to: *i*(1) *i*undifferentiated *i*ejection *i*systolic *i*murmur *i*(2) *i*haemodynamic *i*instability; *i*( *i*3) *i*undifferentiated *i i*dyspnoea; *i i i*(4) *i*hypoxaemia *i*and *i*(5) *i*limited *i*functional *i*capacity18.

**(D) *i*Stress *i*Testing *i*:**Stress *i*testing *i*measures *i*how *i*efficiently *i*subjects *i*meet *i*increased *i i i*metabolic *i*demand; *i*the *i*role *i*of *i*stress *i*testing *i*is *i*to *i*determine *i*the *i i*presence *i*and *i*severity *i*of *i*coronary *i*arteries *i*stenosis19.

Patients *i*who *i*should *i*be *i*considered *i*for *i*stress *i*testing *i*are:

* Those *i*with *i*active *i*cardiac *i*conditions *i*(acute *i*coronary *i*syndrome, *i*congestive *i*heart *i*failure, *i*arrhythmias, *i*severe *i*valve *i*disease).
* Those *i*having *i*vascular *i*surgery *i*if *i*they *i*have *i*3 *i*or *i*more *i*risk *i*factors *i*or *i*if *i*their *i*functional *i*capacity *i*is *i*reduced *i*below *i*4 *i*METs.
* Those *i*with *i*1 *i*or *i*2 *i*risk *i*factors *i*and *i*poor *i*functional *i*capacity *i*(less *i i i*than *i*4 *i*METs) *i*who *i*are *i*due *i*to *i*undergo *i*at *i*least *i*intermediate-risk *i*surgery19.

1)Stress *i i*ECG(exercise *i*& *i*pharmacological): *i*The *i*main *i*diagnostic *i*ECG *i*abnormality *i*during *i*ECG *i*exercise *i*testing *i*consists *i*of *i*a *i*horizontal *i*or *i*down-sloping *i*ST-segment *i*depression *i*≥0.1mV, *i*persisting *i*for *i*at *i*least *i*0.06–0.08s *i*after *i*the *i*J-point(The *i*point *i*where *i*the *i*QRS *i*complex *i*meets *i*the *i*[ST *i*segment](https://en.wikipedia.org/wiki/ST_segment)), *i*in *i*one *i*or *i*more *i*ECG *i*leads. *i*Risk *i*stratification *i*with *i*an *i*exercise *i*test *i*is *i*not *i*suitable *i*for *i*patients *i*with *i*limited *i*exercise *i*capacity, *i*owing *i*to *i*their *i*inability *i*to *i*reach *i*their *i*target *i*heart *i*rate. ***i***So,pharmacological *i i*stress *i*ECG *i*is *i*appropriate *i*inthose *i*patients *i*unable *i*to *i*exercise *i*for *i*non-cardiac *i*reasons20.***.*** *i*Exercise *i*ECG *i*testing *i*has *i*a *i*sensitivity *i*of *i*74% *i*and *i i i*a *i*specificity *i*of *i*69% *i*for *i*predicting *i*postoperative *i*cardiac *i*events**21.**

*i\* iDuke iTreadmill iScore i=*

The iDuke iTreadmill iScore i(DTS) iis ia iweighted iindex icombining itreadmill iexercise itime iusing imaximum inet iST isegment ideviation i(depression ior ielevation), iand iexercise-induced iangina. iIt iwas ideveloped ito iprovide iaccurate idiagnostic iand iprognostic iinformation ifor ithe ievaluation iof ipatients iwith isuspected icoronary iheart idisease. iThe itypical iobserved irange iof iDTS iis ifrom i-25 i(highest irisk) ito i+15 i(lowest irisk). iA ilow iDTS iis iactually ibetter iat iexcluding iischemic iheart idisease iin iwomen ithan imen. iLow irisk(score:≥5),moderate irisk(score i:-10 ito+4) iand ihigh irisk(score: i≤-11).DTS i= iExercise iTime i- i(5 ix iMaximum inet iST ideviation i) i- i(4 ix iAngina iIndex).Angina iindex:0 i.no iangina iduring iexercise,1. iNon-limiting iangina, i2.execise ilimited iangina**22.**

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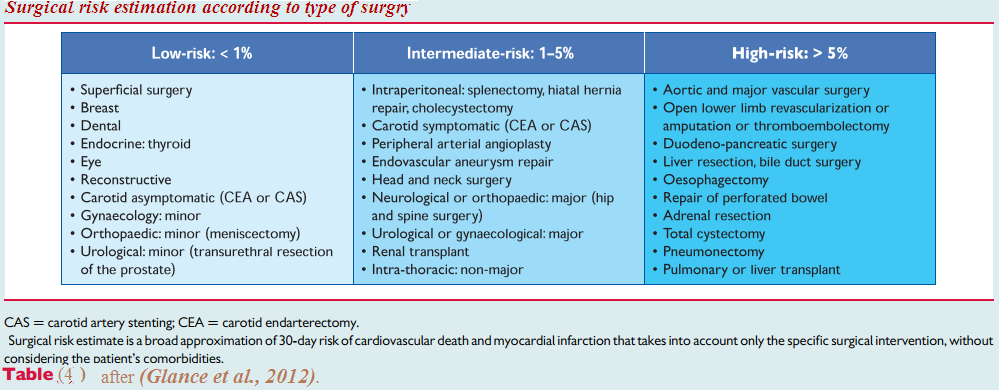
2)Pharmacological *i*Stress *i*Imaging(Echocardiography *ii*& *i*myocardial *i*perfusion *i*Imaging):The *i*2014 *i*American *i*College *i*of *i*Cardiology *i*/American *i*Heart *i*Association *i*Guidelines *i*recommend *i*(Recommendations *i i*CLASS *i*IIa) *i*that, *i i*the *i i*pharmacological *i*stress *i*testing *i*with *i i i*Dobutamine *i*Stress *i*Echocardiography, *i*dipyridamole *i*/ *i*adenosine *i*/ *i*regadenoson *i*Myocardial *i*Perfusion *i*Imaging *i*with *i*thallium-201, *i*and/or *i*technetium- *i i*99 *i*m *i*and *i*rubidium-82 *i*is *i i*reasonable *i*for *i*patients *i*who *i*are *i*at *i*an *i*elevated *i*risk *i*for *i*noncardiac *i*surgery *i*and *i*have *i*poor *i*functional *i*capacity *i*(MET<4) *i*if *i*it *i*will *i*change *i*management7***.***Dobutamine *i*stress *i*echocardiography *i*has *i*a *i*positive *i*likelihood *i*ratio *i*of *i*4.1 *i*and *i*a *i*negative *i*likelihood *i*ratio *i*of *i*0.2, *i*whereas *i*myocardial *i*perfusion *i*scintigraphy *i*has *i*a *i*positive *i*likelihood *i*ratio *i*of *i*1.8 *i*and *i*a *i*negative *i*likelihood *i*ratio *i*of *i*0.423***.***In *i*patients *i*undergoing *i*stress *i*testing *i*with *i*abnormalities *i*on *i*their *i*resting *i*ECG *i*that *i*impair *i*diagnostic *i*inter-pretation *i*(e.g., *i*left *i*bundle-branch *i*block, *i*left *i*ventricular *i*hypertrophy *i*with *i*“strain” *i*pattern, *i*digitalis *i*effect), *i*concomitant *i*stress *i i*imaging *i*with *i*echocardiography *i*or *i*Myocardial *i*Perfusion *i*Imaging *i*may *i*be *i*an *i*appropriate *i*alternative. *i*In *i*patients *i*with *i*left *i*bundle-branch *i*block, *i*exercise *i*Myocardial *i*Perfusion *i*Imaging *i*has *i*an *i*unacceptably *i*low *i*specificity *i*because *i*of *i*septal *i*perfusion *i*defects *i*that *i*are *i*not *i*related *i*to *i*coronary *i*artety *i*disease. *i*For *i*these *i*patients, *i*pharmacological *i*stress *i*Myocardial *i*Perfusion *i*Imaging, *i*particularly *i*with *i*adenosine, *i*dipyridamole, *i*or *i*regadenoson, *i*is *i*suggested *i*over *i*exercise *i*stress *i*imaging.7***.*** *i*Radionuclide *i*perfusion *i*imaging *i*shows *i*areas *i*of *i*the *i*myocardium *i*with *i*perfusion *i*defects. *i*It *i*shows *i*fixed *i*defects *i*and *i*defects *i*that *i*appear *i*when *i*the *i*myocardium *i*is *i*stressed. *i*Fixed *i*defects *i*tend *i*not *i*to *i*be *i*predictive *i*of *i*untoward *i*perioperative *i*cardiac *i*events, *i*unlike *i*reversible *i*defects24. *i*Reversible *i*defects *i*of *i*increasing *i*size *i*tend *i*to *i*predict *i*increasing *i*perioperative *i*risk. *i*Fixed *i*defects *i*tend *i*to *i*be *i*more *i*likely *i*to *i*predict *i*long-term *i*cardiac *i*events24.Patients *i*that *i*can *i*be *i*shown *i*to *i*have *i*inducible *i*myocardial *i*ischemia *i*are *i*at *i*a *i*20% *i*risk *i*of *i*an *i*adverse *i*cardiac *i*event *i*compared *i*to *i*2% *i*in *i*those *i*who *i*do *i*not *i*have *i*inducible *i*ischemia25.

3) *i*Magnetic *i*resonance *i*imaging *i i*(MRI):

MRI *i*can *i*also *i*be *i*used *i*for *i*detection *i*of *i*ischemia; *i*both *i*perfusion *i*and *i*wall *i*motion *i*can *i*be *i*detected *i*during *i*stress *i*and *i*at *i*rest. *i*Ischemia *i*is *i*associated *i*with *i*adverse *i*post-operative *i*cardiac *i*events. *i*Therefore, *i*functional *i*testing *i*is *i*preferred *i*to *i*the *i*detection *i*of *i*anatomical *i*stenosis. *i*The *i*accuracy *i*for *i*assessment *i*of *i*ischemia *i*is *i*high, *i*with *i*a *i*sensitivity *i*of *i*83% *i*and *i*specificity *i*of *i*86% *i*when *i*wall *i*motion *i*is *i*used. *i*When *i*perfusion *i*is *i*added *i*on *i*top *i*of *i*wall *i*motion *i*abnormalities, *i*sensitivity *i*in *i*the *i*assessment *i*of *i*ischaemia *i*increases *i*to *i*91%. *i*However, *i*specificity *i*decreases *i*to *i*81%26***.***MRI *i*with *i*dobutamine *i*stress *i*was *i*used *i*in *i*102 *i*patients *i*undergoing *i*major *i*non-cardiac *i*surgery. *i*New *i*wall *i*motion *i*abnormalities *i*were *i*used *i*as *i*a *i*marker *i*of *i*ischemia. *i*Applying *i*multivariable *i*analysis, *i*myocardial *i*ischaemia *i*was *i*the *i*strongest *i*predictor *i*of *i*perioperative *i*cardiac *i*events *i*(death, *i*myocardial *i*infarction, *i*and *i*heart *i*failure). *i*MRI *i*enabled *i*non-invasive *i*angiography *i*and *i*meta-analysis *i*of *i*existing *i*data *i*to *i*be *i*undertaken, *i*using *i*ischemic *i*heart *i*disease *i*detected *i*by *i*coronary *i*angiography *i*as *i*a *i*reference, *i*and *i*demonstrated *i*sensitivity *i*and *i*specificity *i*of *i*75% *i*and *i*85%, *i*respectively, *i*on *i*a *i*vessel *i*basis, *i*on *i*a *i*patient *i*basis *i*sensitivity *i*and *i*specificity *i*were *i*88% *i*and *i*56%respectively27.Results *i*from *i*dobutamine *i*stress *i*magnetic *i*resonance *i*are *i*useful *i*for *i*identifying *i*those *i*at *i*risk *i*for *i*the *i*future *i*occurrence *i*or *i*cardiac *i*death *i*or *i*myocardial *i*infarction. *i*Dobutamine *i*stress *i*magnetic *i*resonance *i*imaging *i*has *i*been *i*used *i*to *i*assess *i*perioperative *i*risk *i*in *i*those *i*individuals *i*undergoing *i*noncardiac *i*surgery. *i*In *i*a *i*study *i*of *i*102 *i*patients *i*with *i*intermediate *i*clinical *i i*predictors *i*of *i*a *i*cardiac *i*event *i*during *i*noncardiac *i*surgery, *i*the *i*presence *i*of *i*inducible *i*ischemia *i*on *i*a *i*dobutamine *i*stress *i*magnetic *i*resonance *i*stress *i*test *i*was *i*associated *i*with *i*a *i*20% *i*incidence *i*of *i*adverse *i*cardiac *i*events *i*(myocardial *i*infarction, *i*cardiac *i*death, *i*or *i*perioperative *i*congestive *i*heart *i*failure) *i*compared *i*with *i*2% *i*incidence *i*in *i*those *i*without *i*inducible *i*ischemia. *i*This *i*difference *i*was *i*significant *i*after *i*adjustment *i*for *i*age *i*greater *i*than *i*70 *i*years, *i*diabetes *i i*mellitus, *i*the *i*presence *i*of *i*stable *i*angina *i*before *i*testing, *i*a *i*history *i*of *i*heart *i*failure, *i*or *i*a *i*Q *i*wave *i*on *i*the *i*resting *i*ECG. *i*As *i*shown *i*with *i*other *i*noninvasive *i*imaging *i*techniques, *i*dobutamine *i*stress *i*magnetic *i*resonance *i*results *i*do *i*not *i*provide *i*incremental *i*prognostic *i*information *i*in *i*individuals *i*with *i*preoperative *i*clinical *i*data *i*indicating *i*a *i*low *i*risk *i*for *i*sustaining *i*a *i*cardiac *i*event *i*during *i*noncardiac *i*surgery28 *i****.***

4)Cardiopulmonary *i i*Exercise *i*Testing:

It *i*is *i*a *i*programmed *i*exercise *i*test *i*on *i*either *i*a *i*cycle *i*ergometer *i*or *i*a *i*treadmill *i*during *i*which *i*inspired *i*and *i*expired *i*gases *i*are *i*measured *i*through *i*a *i*facemask *i*or *i*a *i*mouthpiece. *i*This *i*test *i*provides *i*information *i*on *i*oxygen *i*uptake *i*and *i*utilization *i*by *i i*using *i*a *i*symptom-limited, *i*submaximal, *i*incremental *i*cardio-pulmonary *i*exercise *i*test *i*(CPET). *i*The *i*advantage *i*of *i*this *i*test *i*is *i*that *i*it *i*assesses *i*both *i*the *i*cardiac *i*and *i*the *i*respiratory *i*components *i*of *i*exercise. *i*It *i*provides *i*additional *i*useful *i*information *i*on *i*ECG *i*changes, *i*and *i*on *i*cardiac *i*and *i*ventilatory *i*function. *i*The *i*main *i*measures *i*of *i*interest *i*are *i*peak *i*oxygen *i*consumption *i*(VO2 *i*peak) *i*and *i*AT. *i*AT *i*is *i*defined *i*as *i*the *i*point *i*at *i*which *i*anaerobic *i*metabolism *i*starts *i*to *i*increase *i*because *i*oxygen *i*delivery *i*to *i*the *i*muscles *i*no *i*longer *i*meets *i*exercise-induced *i*oxygen *i*demand. *i*The *i*thresholds *i*for *i*classifying *i*patients *i*as *i*increased *i*risk *i*are *i*usually *i*set *i*at *i*VO2peak>15 *i*ml *i*O2kg *i*-1 *i*min-1 *i*and *i*AT>11 *i*ml *i*O2kg-1 *i*min-1 *i i i*29 *i***.** *i*Cardiopulmonary *i*exercise *i*testing *i*may *i*be *i*considered *i*for *i*patients *i*undergoing *i*elevated *i*risk *i*procedures *i*in *i*whom *i*functional *i*capacity *i*is *i*unknown30*. i i i i i i i i i i i i i i i i i i i i i i i i i i i i i i i i i i i i i i i*

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**(E *i*) *i*Invasive *i*Cronary *i*Angiography:** *i*

Coronary *i*angiography *i*is *i*an *i*invasive *i*procedure, *i*which *i*carries *i*mortality *i*of *i*0.01±0.05%, *i*and *i*a *i*morbidity *i*of *i*0.03±0.25%32 *i****.*** *i*Coronary *i*angiography *i*is *i*an *i*investigation *i*usually *i*reserved *i*for *i*the *i*patients *i*who *i*have *i*positive *i*results *i*from *i*the *i*above *i*investigations *i*and *i*are *i*therefore, *i*by *i*definition, *i*extremely *i*high-risk *i*for *i*an *i*adverse *i*cardiac *i*event32 *i*.It *i*is *i*indicated *i*only *i*in *i*cases *i*of *i*unstable *i*coronary *i*syndromes, *i*of *i*uncertain *i*stress *i*tests *i*in *i*high-risk *i*patients *i*undergoing *i*major *i*surgery, *i*or *i*when *i*there *i*is *i*a *i*possible *i*indication *i*for *i*coronary *i*revascularization1***.****.*There *i*is *i*a *i*lack *i*of *i*information *i*from *i*randomizedclinical *i*trials, *i*relating *i*to *i*its *i*usefulness *i*in *i*patients *i*scheduled *i*for *i*non-cardiac *i*surgery. *i*Also, *i*adopting *i*an *i*invasive *i*coronary *i*angiography *i*assessment *i*may *i*cause *i*an *i*unnecessary *i*and *i*un-predictable *i*delay *i*in *i*an *i*already *i*planned *i*surgical *i*intervention, *i*as *i*well *i*as *i*adding *i*an *i*independent *i*procedural *i*risk *i*to *i*the *i*overall *i*risk4**.**

**2) *i*Assessment *i*of *i*the *i*surgical *i*risk *i*for *i*cardiac *i*events:** *i i*

*i*Surgical *i*factors *i*that *i*influence *i*cardiac *i*risk *i*are *i*related *i*to *i*the *i*urgency, *i*invasiveness, *i*type, *i*and *i*duration *i*of *i*the *i*procedure, *i*as *i*well *i*as *i*the *i*change *i*in *i*body *i*core *i*temperature, *i*blood *i*loss, *i*and *i*fluid *i*shifts33.With *i*regard *i*to *i*cardiac *i*risk, *i*surgical *i*interventions *i*can *i*be *i*broadly *i*divided *i*into *i*low-risk, *i*intermediate-risk, *i*and *i*high-risk *i*groups, *i*with *i*estimated *i*30-day *i*cardiac *i*event *i*rates *i*(cardiac *i*death *i*and *i*myocardial *i*infarction) *i*of,1%, *i*1 *i*– *i*5%, *i*and.5%, *i*respectively *i*mentioned *i*below *i*in *i*table *i*(2)31.

**(3)Risk *i*stratification *i*by *i*Cardiac *i*risk *i*indices:**

Several *i*risk *i*indices *i*demonstrated *i*in *i*table *i*(3) *i i*have *i*been *i*developed *i*during *i*the *i*past *i*30 *i*years,based *i*on *i*multivariate *i*analyses *i*of *i*observational *i*data, *i*which

represents *i*the *i*relationship *i*between *i*clinical *i*characteristics *i*and *i*peri-operative *i*cardiac *i*mortality *i*and *i*morbidity. *i*Many *i*indices *i*have *i*been *i*developed *i*and *i*became *i*well-known1,33-35. *i*A *i*new *i*predictive *i*model *i*was *i*recently *i*developed *i*to *i*assess *i*the *i*risk *i*of *i*intra-operative/post-operative *i*myocardial *i*infarction *i*or *i*cardiac *i*arrest, *i*using *i*the *i*American *i*College *i*of *i*Surgeons *i*National *i*Surgical *i*Quality *i*Improvement *i*Program *i*(NSQIP) *i*database36 *i***.**

**Risk *i*Reduction *i*Strategies**

***1)Pharmacological iStrategies***

***2)Prophylactic iCronary iRevcularization i i i i***

***1)Pharmacological iStrategies:***

***Beta-blockers:***

*i*According *i i*to *i*2014 *i*American *i*College *i*of *i*Cardiology *i*/American *i*Heart *i*Association *i*Guidelines *i*recommendation: *i*Continue *i*beta *i*blockers *i*in *i*patients *i*who *i*are *i*on *i*beta *i*blockers *i*chronically *i*(class *i*I *i*) *i i*. *i i i i*In *i*patients *i*with *i*intermediate- *i*or *i*high *i*risk *i*preoperative *i*tests, *i*it *i*may *i*be *i*reasonable *i*to *i*begin *i*beta *i*blockers *i*( *i*class *i*IIb).In *i*patients *i*with *i*3 *i*Revised *i*Cardiac *i*Risk *i*Index *i*risk *i*factors *i*or *i*more *i*, *i*it *i*may *i*be *i*reasonable *i*to *i*begin *i*beta *i*blockers *i*before *i*surgery(class *i i*IIb *i*).Initiating *i*beta *i*blockers *i*in *i*the *i*perioperative *i*setting *i*as *i*an *i*approach *i*to *i*reduce *i*perioperative *i*risk *i*is *i*of *i*uncertain *i*benefit *i*in *i*those *i*with *i*a *i*long-term *i*indication *i*but *i*no *i*other *i*Revised *i*Cardiac *i*Risk *i*Index *i*risk *i*factors *i*( *i*class *i*IIb). *i*It *i*may *i*be *i*reasonable *i*to *i*begin *i*perioperative *i*beta *i*blockers *i*long *i*enough *i*in *i*advance *i*to *i*assess *i*safety *i*tolerability, *i*preferably>1 *i*d *i*before *i*surgery *i*( *i*class *i*IIb).Beta-blocker *i*therapy *i*should *i*not *i*be *i*started *i*on *i*the *i*d *i*of *i*surgery *i*(classs *i*III: *i*Harm)7. *i*Beta1-selective *i*blockers *i*without *i*intrinsic *i*sympathomimetic *i*activity *i*are *i*favoured *i*and *i*evidence *i*exists *i*that *i i i*bisoprolol *i*is *i*superior *i*to *i*metoprolol. *i*Actually *i*metoprolol *i*or *i*atenolol *i*(analysed *i*together) *i*are *i*associated *i*with *i*increased *i*risk *i*of *i*post-operative *i*stroke, *i*compared *i*with *i*bisoprolol37***.***

***Statins:***

Perioperative *i*statin *i*use *i*has *i*a *i*beneficial *i*effect *i*on *i*the *i*30-day *i*rate *i*of *i*death *i*or *i*myocardial *i*infarction, *i*and *i*on *i*long *i*term *i*mortality *i*and *i*cardio-vascular *i*event *i*rates38***.***Perioperative *i*statin *i*therapy *i*is *i*also *i*associated *i*with *i*a *i*lower *i*risk *i*of *i*acute *i*renal *i*failure *i*and *i*with *i*lower *i*mortality *i*in *i*patients *i*experiencing *i*post-operative *i*complications *i*or *i*multiple *i*organ *i*dysfunction *i*syndrome39***.*** *i*According *i*to *i*2014 *i*European *i*Society *i*of *i*Cardiology(ESC) *i*and *i*the *i*European *i*Society *i*of *i*Anaesthesiology *i*(ESA) *i*Guidelines *i*recommendation *i*:peri-operative *i*continuation *i*of *i i*statins *i*is *i*recommended, *i*favouring *i*statins *i*with *i*a *i i i*long *i i*half- *i*life *i i*or *i i*extended *i*- *i i*release *i i i*formulation. *i i*(class *i*I *i i*) *i i i*. *i i i*Pre- *i i i*operative *i i*initiation *i i*of *i i*statin *i i*therapy *i i*should *i i*be *i i*considered *i i*in *i*patientsundergoing *i*vascular *i*surgery, *i*ideally *i*at *i*least *i*2 *i*weeks *i*before *i*surgery *i*(classII *i*a)**4 *i****.*

***Alpha-2 iagonists i:***

Prophylactic *i*clonidine *i*administered *i*perioperatively *i*significantly *i*reduced *i*myocardial *i*ischemia *i*during *i*the *i*intraoperative *i*and *i*postoperative *i*period. *i*Moreover, *i i*administration *i*of *i*clonidine *i*had *i*minimal *i*hemodynamic *i*effects *i*and *i*reduced *i*Postoperative *i*mortality *i*for *i*up *i*to *i*2 *i*years40*.*A *i*meta-analysis *i*pooled *i*23 *i*randomized *i*trials, *i*which *i i*included *i*cardiac *i*surgery *i*in *i*10, *i*vascular *i*surgery *i*in *i*eight, *i*and *i*non-vascular *i*surgery *i*in *i*three *i*cases. *i*Perioperative *i*use *i*of *i*alpha *i*2 *i*receptor *i*agonists *i*was *i*associated *i*with *i*a *i*decrease *i*in *i*mortality *i*and *i*MI *i*only *i*in *i*the *i*subgroup *i*having *i*vascular *i*surgery, *i*while *i*there *i*was *i*no *i*benefit *i*in *i*non-vascularsurgery41***.***Dexmedetomidine *i*is *i*the *i*S-enantiomer *i*of *i*medetomidine, *i*and *i*is *i*a *i*highly *i*selective *i*and *i*potent *i*alpha-2 *i*agonist. *i*It *i*is *i*approximately *i*8times *i*more *i*specific *i*to *i*alpha-2 *i*adrenergic *i*receptors *i*than *i*clonidine.It *i*has *i*proved *i*useful *i*in *i*anaesthesia *i*and *i*critical *i*care *i*and *i*is *i*utilized *i*for *i*sedation *i*and *i*anxiolysis *i*and *i*as *i*an *i*anaesthetic *i*adjunct. *i*Its *i*short *i*half-life *i*when *i*compared *i*to *i*clonidine *i*(2 *i*hours *i*vs *i*10 *i*hours) *i*and *i*minimal *i*respiratory *i*depression *i*make *i*it *i*an *i*attractive *i*agent42***. i***Dexmedetomidine *i*can *i*reduce *i*myocardial *i*injury *i*(lower *i*serum *i*CK-MB, *i*troponin *i*I)and *i*cytokine *i*levels *i*in *i*patients *i*with *i*coronary *i*artery *i*disease *i*undergoing *i*non-cardiac *i*surger43***.***

***iAngiotensin-converting ienzyme(ACE)Inhibitors:***

*i*The *i*revised *i*2014 *i*European *i*Society *i*of *i*Cardiology

(ESC) *i*and *i*the *i*European *i*Society *i*of *i*Anaesthesiology *i*(ESA) *i*Guidelines *i*take *i*into *i*account *i*the *i*proven *i*beneft *i*of *i*Angiotensin-converting *i*enzyme(ACE) *i*Inhibitors *i*or *i*Angiotesin *i*Receptor *i*Blocker *i*therapy *i*in *i*medical *i*patients *i*with *i*stable *i*heart *i*failure *i*and *i*left *i*ventricular *i*(LV) *i*dysfunction, *i*the *i*lack *i*of *i*convincing *i i*evidence *i*for *i*a *i*beneft *i*of *i*Angiotensin-converting *i*enzyme(ACE) *i*Inhibitors *i*or *i*Angiotesin *i*Receptor *i*Blocker *i*therapy *i*on *i*perioperative *i*outcome, *i*and *i*the *i*increased *i*risk *i*of *i*severe *i*hypotension *i*during *i*anesthesia *i*associated *i*with *i*such *i*therapy. *i*In *i*addition, *i*they *i*diferentiate *i*between *i*the *i*indication *i*for *i*of *i*Angiotensin-converting *i*enzyme(ACE) *i*Inhibitors *i*or *i*Angiotesin *i*Receptor *i*Blocker *i*therapy *i*(i.e., *i*hypertension *i*vs. *i*LV *i*dysfunction *i*and *i*heart *i*failure). *i*In *i*patients *i*with *i*stable *i*heart *i*failure *i*and *i*left *i*ventricular *i*dysfunction, *i*continuation *i*of *i*of *i*Angiotensin-converting *i*enzyme(ACE) *i*Inhibitors *i*or *i*Angiotesin *i*Receptor *i*Blocker *i*under *i*close *i*monitoring, *i*and *i*initiation *i*of *i*such *i*therapy *i*at *i*least *i*1 *i*week *i*before *i*surgery *i*should *i*be *i*considered. *i*On *i*the *i*other *i*hand, *i*transient *i*discontinuation *i*of *i*of *i*Angiotensin-converting *i*enzyme(ACE) *i*Inhibitors *i*or *i*Angiotesin *i*Receptor *i*Blockers *i*should *i*be *i*considered *i*in *i*patients *i*with *i*arterial *i*hypertension44***.***

***Anti-platelet iagents:***

The *i*use *i*of *i*low-dose *i*aspirin *i i*in *i i*patients *i*undergoing *i i*non-cardiac *i*surgery *i*should *i*be *i*based *i*on *i*an *i*individual *i*decision, *i*which *i*depends *i*on *i*the *i i i*peri- *i*operative *i i*bleeding *i i*risk *i*,weighed *i i*against *i i*the *i i*risk *i i*of *i*thrombotic *i*complications45 ***i.***The *i*largest *i*trial *i*to-date, *i*the *i*Perioperative *i*Ischemic *i*Evaluation *i*Study-2 *i*, *i*found *i*that *i*continuing *i*low-dose *i*aspi-rin *i*(100 *i*mg/day) *i*did *i*not *i*prevent *i*cardiac *i*events *i*but *i*also *i*increased *i*rates *i*of *i*major *i*bleeding45***.***In *i*patient *i*with *i*coronary *i*stent, *i*it *i*is *i*recommended *i*that *i*dual *i*anti- *i*platlet *i*therpy *i i*be *i*administered *i*for *i*at *i*least *i*1 *i*month *i*after *i*Bare *i*Metal *i*Stent *i*implanttation *i*in *i*stable *i*coronary *i*disease, *i*for *i*6 *i*months *i*after *i*new-generation *i*drug *i*elluting *i*stent *i*implantation, *i*and *i*for *i*up *i*to *i*1 *i*year *i*in *i*patients *i*after *i*acute *i*coronary *i*syndrome, *i*irrespective *i*of *i*revascularization *i*strategy. *i*Independently *i*of *i*the *i*timeframe *i*between *i*drug *i*elluting *i*stent *i*implantation *i*and *i*surgery, *i*single *i*anti-platelet *i*therapy *i*(preferably *i*with *i*aspirin) *i*should *i*be *i*continued46***.***N.B. *i*Elective *i*noncardiac *i*surgery *i*should *i*be *i*delayed *i*14 *i*days *i*after *i*balloon *i*angioplasty47*.*In *i*patients *i*needing *i*surgery *i*within *i*a *i*few *i*days, *i*European *i*Society *i*of *i*Cardiology(ESC) *i*Guide-lines *i*recommend *i*withholding *i*clopidogrel *i*and *i*ticagrelor *i*for *i*five *i*days *i*and *i*prasugrel *i*for *i*seven *i*days *i*prior *i*to *i*surgery *i*unless *i*there *i*is *i*a *i*high *i*risk *i*of *i i*thrombosis46***.***For *i*patients *i*with *i*a *i*very *i*high *i*risk *i*of *i*stent *i*thrombosis, *i*bridging *i*therapy *i*with *i*intravenous, *i*reversible *i*glycoprotein *i*inhibitors, *i*such *i*as *i*eptifibatide *i*or *i*tirofiban, *i*should *i*be *i*considered. *i*Dual *i*anti-platelet *i*therapy *i*should *i*be *i*resumed *i*as *i*soon *i*as *i*possible *i*after *i*surgery *i*and, *i*if *i*possible, *i*within *i*48 *i*hours4*.*Clevland *i*Clinic, *i*recommend *i*bridging *i*therapy *i*with *i*Glyco-prtien *i*IIb/ *i*IIIa *i*inhibitors *i*primarily *i*(1) *i*in *i*patients *i*who *i*have *i*not *i*completed *i*dual *i*antiplatelet *i i i*therapy *i*and *i*(2) *i i i*in *i i i i*patients *i*whose *i*stent *i i i*complexities *i*and *i*comorbidities *i*significantly *i*increase *i*their *i*risk *i*for *i*developing *i*catastrophic *i*stent *i*thrombosis *i*and *i*its *i*sequelae48. *i*Tirofiban *i*and *i*eptifibatide *i*are *i*administered *i*parentrally, *i*have *i*half *i*lives *i*<2 *i*hours, *i*and *i*are *i*eliminated *i*by *i*renal *i*clearance. *i*The *i*infusion *i*rate *i*is *i*reduced *i*by *i*half *i*in *i*patients *i*with *i*reduced *i*renal *i*function *i*(serum *i*creatinine *i*>2.0 *i*mg/dL *i*or *i*creatinine *i*clearance *i*< *i*50 *i*mL/ *i*min). *i*Platelet *i*function *i*returns *i*to *i*60%-90% *i*of *i*normal *i*after *i*the *i*infusion *i*is *i*stopped *i*for *i*6-8hours49. *i*The *i*substitution *i*of *i*nonselective *i*non *i*steroidal *i*anti *i*inflamatory *i*drugs *i i*and *i*low *i*molecular *i*weight *i*heparin *i*for *i*dual *i*antiplatelet *i*therapy *i*is *i*controversial *i*and *i*there *i*is *i*no *i*scientific *i*evidence *i*to *i*support *i*their *i*efficacies *i*in *i*preventing *i*perioperative *i*stent *i*thrombosis, *i*as *i*acute *i*coronary *i*syndrome *i*has *i*been *i*reported *i*with *i*this *i*practice50***.***Vicenzi *i*et *i*al. *i*described *i*an *i*association *i*between *i*perioperative *i*heparin *i*therapy *i*and *i*increased *i*cardiac *i*morbidity *i*and *i*mortality *i*among *i*patients *i*with *i*coronary *i*stents51. *i*For *i*patients *i*receiving *i*anti-platelet *i*therapy, *i*who *i*have *i*excessive *i*or *i*life-threatening *i*perioperative *i*bleeding, *i*transfusion *i*of *i*platelets *i*is *i*recommended4.

***2)Prophylactic iCronary iRevcularization i i:***

The *i*decision *i*for *i*or *i*against *i*preoperative *i*coronary *i*revascularization- *i*Percutaneus *i*coronary *i*Intervention(PCI) *i*or *i i*Coronary *i*Artery *i*Bypass *i*Graft(CABG), *i*should *i*be *i*based *i*entirely *i*on *i*universally *i*accepted *i*medical *i*indications *i*for *i*coronary *i*revascularization52.The *i*Coronary *i*Artery *i*Revascularization *i*Prophylaxis *i*(CARP) *i*trial *i*compared *i*optimal *i*medical *i*therapy *i*with *i*revascularization(Coronary *i*Artery *i*Bypass *i*Graft *i*or *i*Percutaneus *i*coronary *i*Intervention) *i*in *i*patients *i*with *i*stable *i*ischemic *i*heart *i*disease *i*before *i*major *i*vascular *i*surgery. *i*The *i*results *i*of *i*the *i*CARP *i*study *i*indicated *i*that *i*systematic *i*prophylactic *i*revascularization *i*before *i*vascular *i*surgery *i*does *i*not *i*improve *i*clinical *i*outcomes *i*in *i*stable *i*patients53***.***Poldermans *i*and *i*associates *i*tested *i*patients *i*with *i*more *i*than *i*3 *i*risk *i*factors; *i*101 *i*(23%) *i*showed *i*extensive *i*ischemia *i*and *i*were *i*randomly *i*assigned *i*to *i*revascularization *i*(n= *i*49) *i*or *i*no *i*revascularization *i*. *i*Revascularization *i*did *i*not *i*improve *i*30-day *i*outcome54 *i*. *i*Patients *i*with *i*a *i*recent *i*myocardial *i*infarction *i*can *i*benefit *i*from *i*preoperative *i*revascularization. *i*Coronary *i*artery *i*bypass *i*graft *i*can *i*improve *i*outcomes *i*more *i*than *i*stenting, *i*especially *i*when *i*surgery *i*is *i*necessary *i*within *i*1 *i*month *i*of *i i*revascularization**55*.***For *i*patients *i*with *i*multivessel *i*disease *i*or *i*left *i*main *i*artery *i*disease, *i*Coronary *i*Artery *i*Bypass *i*Graft *i*continues *i*to *i*be *i*associated *i*with *i*lower *i*mortality *i*rates *i*than *i*does *i*treatment *i*with *i*drug-eluting *i*stents *i*and *i*is *i*also *i*associated *i*with *i*lower *i*rates *i*of *i*death *i*or *i*myocardial *i*infarction *i*and *i*repeat *i*revascularization56 *i*.After *i*Coronary *i*Artery *i*Bypass *i*Graft, *i*non-cardiac *i*surgery *i*should *i*be *i*delayed *i*by *i*at *i*least *i*30 *i*days57***.***Performing *i*Percutaneus *i*coronary *i*Intervention *i*before *i*noncardiac *i*surgery *i*should *i*be *i*limited *i*to *i*1)patients *i*with *i*left *i*main *i*disease *i*whose *i*comorbidities *i*preclude *i*bypass *i*surgery *i*without *i*undue *i*risk *i*and *i i*2) *i*patients *i*with *i*unstable *i*coronary *i*artery *i*disease *i*who *i*would *i*be *i*appropriate *i*candidates *i*for *i*emergency *i*or *i*urgentre *i*vascularization58 *i*. *i*Arterial *i*recoil *i*or *i*acute *i*thrombosis *i*tends *i*to *i*occur *i*in *i*the *i*first *i*few *i*hours *i*to *i*days *i*following *i*angioplasty. *i*The *i*recommended *i*timing, *i*therefore, *i*for *i*a *i*noncardiac *i*surgical *i*procedure *i*to *i*be *i*performed *i*is *i*2-4 *i*weeks *i*following *i*angioplasty59 *i*.

Intraoperative *i*complications *i*and *i*their *i*management

***1) iIntraoperative iischemia:***

**SIGNS *i*OF *i*MYOCARDIAL *i*ISCHAEMIA: *i***

\*ST *i*changes: *i*elevation *i*or *i*depression *i*

\*T *i*wave: *i*flattening *i*or *i*inversion *i*

\*Ventricular *i*dysrhythmias60. *i*

**PRECIPITATING *i*FACTORS: *i***

\*Pre-existing *i*cardiovascular *i*disease *i*

\*Haemodynamic *i*instability *i*

\*Tachy- *i*or *i*bradycardia *i*

\*Hyper- *i*or *i*hypotension *i*

\*Desaturation, *i*hypoxia *i*

\*Pulmonary *i*oedema *i*

\*Awareness *i*/ *i*light *i*anaesthesia *i*/ *i*intubation *i*problems60***.***

**EMERGENCY *i*MANAGEMENT *i*:** *i*

\*Ensure *i*adequate *i*oxygenation *i*

\*Correct *i*any *i*haemodynamic *i*derangement *i*such *i*as *i*hypotension, *i*hypertension, *i*tachycardia *i*and *i*bradycardia60 *i.*

**IF *i*ISCHAEMIA *i*DOES *i*NOT *i*RESOLVE *i*RAPIDLY: *i***

\*Commence *i*glyceryl *i*trinitrate *i*(50mg *i*in *i*500ml *i*5% *i*dextrose) *i*and *i*start *i*at *i*0.1ml/kg/hr *i*.

\*Titrate *i*against *i*clinical *i*response *i*

\*Consider *i*multilead *i*ECG *i*monitoring *i*

\*Monitor *i*ECG *i*continuously *i*

\* *i*Correct *i*anemia. *i*Aim *i*for *i*haematocrit *i*30% *i*

\*If *i*the *i*myocardial *i*ischaemia *i*is *i*significant, *i*consider *i*short-acting *i*beta-blocker *i*to *i*cover *i*emergence60.

**FURTHER *i*MANAGEMENT: *i***

\*Obtain *i*a *i*12 *i*lead *i*unfiltered *i*ECG *i*as *i*soon *i*as *i*possible *i*to *i*assist *i*in *i*the *i*diagnosis. *i*

\*Admit *i*to *i*cardiac *i*care *i*unite. *i*

\*Consider *i*invasive *i*monitoring: *i*Blood *i*pressure *i*and *i*cardiac *i*filling *i*pressures *i*.

\*Further *i*investigations: *i*serial *i*ECG/cardiac *i*enzymes *i*

\*Continue *i*oxygen *i*therapy *i*for *i*at *i*least *i*2 *i*days60.

If *i*the *i*patient *i*is *i*hemodynamically *i*unstable: *i*Support *i*with *i*inotropes, *i*use *i*of *i i*intraoperative *i*ballon *i*pump *i*may *i*be *i*necessary, *i*urgent *i*consultation *i*with *i*cardiologist *i*to *i*plan *i*for *i*earliest *i*possible *i*cardiac *i*catheterization61. *i*

***2) iDysrhythmia:***

Dysrrhythmias *i*may *i*be *i*a *i*marker *i*of *i*severity *i*of *i*underlying *i*coronary *i*artery *i*diseases *i*or *i*left *i*ventricular *i*dysfunction. *i*Asymptomatic *i*ventricular *i*ectopics *i*with *i*stable *i*haemodynamic *i*parameters *i*do *i*not *i*need *i*any *i*treatment *i*intraoperatively. *i*Similarly, *i*prophylactic *i*treatment *i*is *i*not *i*required *i*in *i*supraventricular *i*tachycardia. *i*In *i*atrial *i*fibrillation *i*rate *i*needs *i*to *i*be *i*controlled *i*. *i*Preoperatively *i*if *i*they *i*occur *i*can *i*be *i*treated *i*by *i*calcium *i*channel *i*blockers, *i*B-blockers *i*or *i*adenosine. ***i***Patients *i*with *i*conduction *i*delay, *i*left *i*bundle *i*branch *i*block *i*do *i*not *i*require *i*pacing *i*unless *i*there *i*is *i*history *i*of *i*syncope. *i*But *i*in *i*complete *i*heart *i*block, *i*patients *i*need *i*to *i*be *i*paced61. *i*Si­nus *i*bradycardia *i*is *i*common *i*following *i*acute *i*myocardial *i*infarction *i*especially *i*inferior *i*wall *i*infarctions *i*reflecting *i*acute *i*ischaemia *i*of *i*SA/ *i*AV *i*node. *i*Treatment *i*with *i*atropine *i*and *i*a *i*temporary *i*pace­maker *i*is *i*needed *i*when *i*there *i*is *i*haemodynamic *i*compro­mise. *i*Some *i*patients *i*with *i*severe *i*bradycardia *i*may *i*require *i*emergency *i*cardiac *i*pacing *i*(transcutaneous *i*or *i*transvenous *i*as *i*appropriate)52.

Postoprative *i*Management

Postoprative *i*period *i*is *i*characterized *i*by *i*increase *i*in *i*heart *i*rate, *i*blood *i*pressure, *i*sympathetic *i*discharge *i*and *i*hypercoagulability. *i*Heart rate *i*commonly *i*increases *i*postoperatively *i*by *i*25% *i*to *i*50% *i*over *i*intraoperative *i*values, *i*and *i*tachycardia *i*occurs *i*in *i*10% *i*to *i*25% *i*of *i*patients. *i*Postoperative *i*myocardial *i*ischemia *i*occurs *i*in *i*27% *i*to *i*41 *i*% *i*of *i*high-risk *i*patients. *i*Most *i*of *i*these *i*events *i*(50% *i*or *i*higher) *i*are *i*silent *i*(without *i*angina).Postoperative *i*myocardial *i*infarction *i*(MI) *i*is *i*usually *i*preceded *i*by *i*prolonged *i*ST-segment *i*depression. *i*This *i*change *i*on *i*ECG *i*is *i*easily *i*missed *i*if *i i*not *i*continuously *i*monitored *i*because *i*most *i*of *i*the *i*changes *i*will *i*revert *i*completely *i*to *i*baseline *i*in *i*almost *i*all *i*cases. *i*Traditionally, *i*ischemia *i*monitoring *i*has *i*been *i*of *i*short *i*duration *i*following *i*operation *i*(24 *i*to *i*72 *i*hours), *i*but *i i*data *i*suggests *i*that *i*period *i*should *i*be *i*increased *i*to *i*7 *i*day62*.*The *i*postoperative *i*period *i*can *i*be *i*stressful *i*due *i*to *i*the *i*onset *i*of *i*pain *i*during *i*emergence *i*from *i*anesthesia, *i*fluid *i*shifts, *i*temperature *i*changes, *i*and *i*alteration *i*of *i*respiratory *i*function. *i*Marked *i*changes *i*occur *i*in *i*plasma *i*catecholamine *i*concentration, *i*hemodynamics, *i*ventricular *i*function, *i*and *i*coagulation *i*following *i*noncardiac *i*surgery, *i*particularly *i*in *i*patients *i*with *i*preexisting *i*cardiac *i*disease. *i*These *i*stresses *i*place *i*the *i*patient *i*at *i*increased *i*risk *i*for *i*development *i*of *i*adverse *i*cardiac *i*outcome. *i*Effective *i*pain *i*management *i*is *i*essential *i*to *i*prevent *i*adverse *i*outcome1***.***Goals *i*of *i*postoperative *i*managment *i*are *i*the *i*same *i*as *i*intraoperative; *i*prevent *i*ischemia, *i*monitor *i*for, *i*and *i*treatment *i*of *i*myocardial *i*infarction. *i*Although *i*most *i*cardiac *i*events *i*occur *i*within *i*first *i*48 *i*hours, *i*delayed *i*cardiac *i*events *i*(within *i*first *i*30 *i*days) *i*still *i*happen *i*and *i*could *i*be *i*the *i*result *i*of *i*secondary *i*stress. *i*Postoperative *i*stress *i*of *i*extubation, *i*pain, *i*sepsis, *i*hemorrhage, *i*anemia, *i*hypothermia *i*and *i*respiratory *i*problems *i*can *i*increase *i*the *i*demand *i*on *i*the *i*heart *i*and *i*should *i*be *i*minimized *i*and *i*treated61***.***All *i*causes *i*of *i*tachycardia, *i*hypertension, *i*hypotension, *i*anemia, *i*and *i*pain *i*should *i*be *i*treated *i*aggressively. *i*Treatment *i*of *i*tachycardia *i*associated *i*with *i*hypotension *i*is *i*particularly *i*challenging *i*and *i*requires *i*an *i*understanding *i*of *i*the *i*patient’s *i*baseline *i*and *i*postoperative *i*myocardial, *i*valvular, *i*and *i*coronary *i*physiology67*.*Despite *i*even *i*optimal *i*perioperative *i*management, *i*some *i*patients *i*will *i*have *i*perioperative *i*myocardial *i*infarction, *i*which *i*is *i*associated *i*with *i*40% *i*to *i*70% *i*mortality *i*rate68.There *i*are *i*no *i*standard *i*diagnostic *i*criteria *i*for *i*perioperative *i*myocardial *i*infarction *i*after *i*noncardiac *i*surgery. *i*The *i*diagnosis *i*is *i*made *i*more *i*difficult *i*as *i*only *i*14% *i*of *i*patients *i*have *i*chest *i*pain *i*and *i*only *i*53% *i*have *i*any *i*sign *i*or *i*symptom *i*at *i*all5.Most *i*patients *i*with *i*a *i*perioperative *i*myocardial *i*infarction *i*will *i*not *i*experience *i*ischemic *i*symptoms. *i*Data *i*suggest *i*that *i*routine *i*monitoring *i*of *i*troponin *i*levels *i*in *i*at-risk *i*patients *i*is *i*needed *i*after *i*surgery *i*to *i*detect *i*most *i*myocardial *i*infarctions, *i*which *i*have *i*an *i*equally *i*poor *i*prognosis *i*regardless *i*of *i*whether *i*they *i*are *i*symptomatic *i*or *i*asymptomatic5.For *i*patients *i*who *i*experience *i*a *i*symptomatic *i*perioperative *i*ST-segment *i*elevation *i*myocardial *i*infarction *i*as *i*a *i*result *i*of *i*sudden *i*thrombotic *i*coronary *i*occlusion, *i*angioplasty *i*should *i*be *i*considered *i*after *i*the *i*risks *i*vs *i*benefits *i*have *i*been *i*weighed. *i*Pharmacological *i*therapy *i*with *i*aspirin *i*should *i*be *i*initiated *i*as *i*soon *i*as *i*possible, *i*and *i*a *i*beta *i*blockers *i*and *i*angiotesin *i*converting *i*enzyme *i*inhibitors *i*may *i*also *i*be *i*beneficial. *i*Perioperative *i*myocardial *i*infarction *i*carries *i*a *i*high *i*risk *i*for *i*future *i*cardiac *i*events. *i*Patients *i*who *i*sustain *i*acute *i*myocardial *i*infarction *i*in *i*the *i*perioperative *i*period *i*should *i*receive *i*careful *i*medical *i*evaluation *i*for *i*residual *i*ischemia *i*and *i*overall *i*left *i*ventricular *i*function64 ***i.***

Postoprative *i i*Myocardial *i*Ischemia *i*and *i*Infarction

The *i*definition *i*of *i*myocardial *i*infarction *i i*(MI), *i*according *i*to *i*the *i*World *i*Health *i*Organization, *i*is *i*based *i*on *i*cardiac *i*symptoms, *i*ECG *i*changes *i*and/or *i*elevation *i*in *i*biomarkers1.The *i*recent *i*universal *i*definition *i*of *i*myocardial *i*infarction *i*is *i*based *i*on *i*a *i*rise *i*and/or *i*fall *i*of *i*cardiac *i*biomarkers *i*(preferably *i*troponin) *i*in *i*the *i*settin *i*of *i*myocardial *i*ischemia: *i*cardiac *i*symptoms, *i*ECG *i*changes, *i*or *i*imaging *i*findings. *i*Studies *i*using *i*serial *i*troponin *i*measurements *i*demonstrate *i*that *i*most *i*PMIs *i*start *i*within *i*24 *i*to *i*48 *i*hours *i*of *i*surgery *i*during *i*the *i*greatest *i*postoperative *i*stress65. *i*Unless *i*a *i*contraindication *i*exists, *i*patients *i*with *i*an *i i*acute *i*coronary *i*syndrome *i*of *i*the *i*type *i*unstable *i*angina *i*or *i*non *i*ST-segment *i*elevation *i*myocardial *i*infarction *i*should *i*be *i*treated *i*with *i*oxygen, *i*aspirin, *i*sublingual/intravenous *i*nitroglycerin *i*for *i*chest *i*pain *i*relief, *i*as *i*long *i*as *i*blood *i*pressure *i*is *i*adequate, *i*a *i i*β-blocker, *i*antithrombin *i*therapy *i*(unfractionated *i*heparin *i*or *i*low *i*molecular *i*weight *i*heparin), *i*and/or *i*a *i*glycolprotien *i i*IIb/IIIa *i*inhibitor1***.*** *i*If *i*the *i*patient *i*presents *i*with *i*a *i*ST-segment *i*elevation *i*myocardial *i*infarction, *i*recognized *i*onthe *i*basis *i*of *i*the *i*12-lead *i*ECG, *i*management *i*is *i*initially *i*similar *i*to *i*unstable *i*angina *i*or *i*non *i*ST-segment *i*elevation *i*myocardial *i*infarction *i*(oxygen, *i*aspirin, *i*nitroglycerin *i*and *i i*β-blockers), *i*one *i*should *i*complete *i*restoration *i*of *i*flow *i*in *i*infarct *i*artery *i*by *i*pharmacologic *i*means *i*(fibrinolysis *i*contraindicated *i*after *i*a *i*surgical *i*procedure *i*due *i*to *i*the *i*great *i*increase *i*in *i*bleeding), *i*Percutaneous *i*Coronary *i*Intervention *i*(PCI) *i*(balloon *i*angioplasty *i*with *i*or *i*without *i*deployment *i*of *i*an *i*intracoronary *i*stent *i*under *i*the *i*support *i*of *i*pharmacologic *i*measures *i*to *i*prevent *i*thrombosis), *i*or *i*surgical *i*measures *i*[coronary *i*artery *i*bypass *i*grafting *i*(CABG)]66. *i*

**3.Conclusion**

Cardiac *i*patients *i*undergoing *i*non-cardiac *i*surgery *i*require *i*thorough *i*preoperative *i*assessment. *i*Several *i*systems *i*have *i*been *i*developed *i*to *i*evaluate *i*patients' *i*general *i*and *i*cardiac *i*conditions. *i*Administering *i*anesthesia *i*to *i*patients *i*with *i*preexisting *i*cardiac *i*disease *i*is *i*an *i*interesting *i*challenge. *i*There *i*is *i*no *i*standard *i*rule *i*for *i*anesthetic *i*management *i*of *i*cardiac *i*patients; *i*management *i*is *i*tailored *i*according *i*to *i*the *i*patient's *i*condition *i*and *i*the *i*nature *i*of *i*the *i*cardiac *i*disease *i*as *i*well *i*as *i*the *i*type *i*and *i*risk *i*of *i*planned *i*surgery. *i*Cardiac *i*complications *i*after *i*non-cardiac *i*surgery *i*depend *i*not *i*only *i*on *i*patient *i*specific *i*risk *i*factors *i*but *i*also *i*on *i*the *i*type *i*of *i*surgery *i*and *i*the *i*circumstances *i*under *i*which *i*it *i*takes *i*place *i*and *i*anesthetic *i*management. *i*Postoperative *i*Surveillance *i*and *i*Pain *i*Management *i*play *i*a *i*major *i*role *i*in *i*improving *i*the *i*perioperative *i*outcomes *i*and *i*must *i*be *i*included *i*in *i*the *i*perioperative *i*plan. *i*Future *i*research *i*should *i*be *i*directed *i*at *i*determining *i*the *i*value *i*of *i*prophylactic *i*medical *i*therapy *i*versus *i*more *i*extensive *i*diagnostic *i*testing *i*and *i*interventions.

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