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The aged cardiovascular risk patient

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Saturday, June 6, 2009 13:00 - 13:45 Room: White 2

Introduction

In The Netherlands the ageing of the population will peak in approximately 30 years time. According to Dutch national healthcare statistics, 25% of the estimated 17 million inhabitants will then be aged > 65. Annually, 4% of the Dutch population is scheduled for a major surgical procedure, with an average peri-operative mortality rate of 1.9% for non day-case procedures. Currently, almost 60% of these surgical patients are aged > 65 [1].

Elderly patients undergoing major non-cardiac surgical procedures are at increased risk of complications during the surgical period such as pneumonia, systemic inflammation, renal impairment, myocardial infarction, congestive heart failure or death. It is estimated that out of all peri-operative complications, cardiac events contribute to 30% of adverse events leading to death. As a result, more than 2,100 older patients die each year due to cardiac complications of non-cardiac surgery in The Netherlands alone.

Pathophysiology of adverse cardiac events

Peri-operative myocardial infarction is the most frequent fatal cardiac complication during non-cardiac surgery. The pathophysiological mechanisms underlying peri-operative myocardial infarction are not completely clear, but seem to be associated with atherogenic coronary artery disease (CAD).

Early atherogenesis is characterised by plaque formation due to accumulation of lipids and recruitment of inflammatory cells in the intima layer of the coronary artery wall. Continuing conditions of dyslipidaemia and inflammation of the vessel wall result in a lipid-core, separated from the vessel lumen by a thin fibrous vulnerable endothelial cap. This thin cap is susceptible to rupture due to increased levels of stress hormones during and after surgery. When the vulnerable coronary plaque ruptures, the liquid lipid core enters the vessel lumen and leads to thrombus formation, (partial) coronary artery occlusion and subsequent myocardial infarction. In patients with fixed stenotic coronary lesions due to advanced atherogenesis, the coronary lumen is narrowed. The narrow lumen limits the maximum flow through the vessel in situations of increased oxygen demand of the myocardium (such as tachycardia in response to pain or bleeding). Insufficient coronary blood flow can induce an oxygen supply/demand mismatch, which results in myocardial ischaemia and eventually in myocardial infarction [2]. Surgery and anaesthesia related factors initiate inflammatory and hypercoagulable states in the patient. Increased levels of circulating inflammatory cells infiltrate the pre-existing atheromatous coronary plaques. The stress state of the patient during surgery induces coronary artery shear stress, and contributes to plaque instability and rupture. Circulating coagulation factors induce thrombus formation at the side of the ruptured plaque, which occludes the vessel and prohibits coronary blood flow. Major increases in blood pressure, heart rate and contractility of the heart caused by the increased stress state of the patient, lead to increases in oxygen demand of the myocardium. Insufficient coronary blood flow due to a narrowed lumen induces myocardial oxygen debt and infarction.

Identifying patients at risk

Pre-operative cardiac risk stratification is used to identify patients at increased risk for such peri-operative cardiac complications. It reveals important information on the status of the patient, the presence and extent of coronary artery disease and other medical risk factors. Being able to identify patients at increased risk for adverse cardiac events provides the peri-operative physician with an important tool to make easier treatment decisions that may affect short and long term outcome of the surgical patient.

Patient characteristics and type of surgery

Pre-operative cardiovascular risk stratification is primarily based on clinical risk factors and type of surgical procedure (Tables 1 and 2). In patients at increased risk, the presence and extent of coronary disease can be evaluated by additional testing (Figure 1). Advanced age is accompanied by an increased prevalence of co-morbidities. As a result, elderly patients are more likely to have (asymptomatic) CAD and are at risk of peri-operative cardiac complications. Previous studies have identified advanced age as an independent predictor of cardiac morbidity and mortality. A recent study of a 10-yr surgical cohort of more than 100 000 Dutch non-cardiac surgical patients found that peri-operative cardiac mortality progressively increased with advanced age (Table 3). Including age in clinical indices to estimate risk of adverse events in patients undergoing non-cardiac surgery was associated with additional prognostic value (C-statistic improved from 0.63 to 0.85) [3].

Table 1

Clinical predictors of increased peri-operative cardiovascular risk (combined risk of cardiac death, nonfatal myocardial infarction)

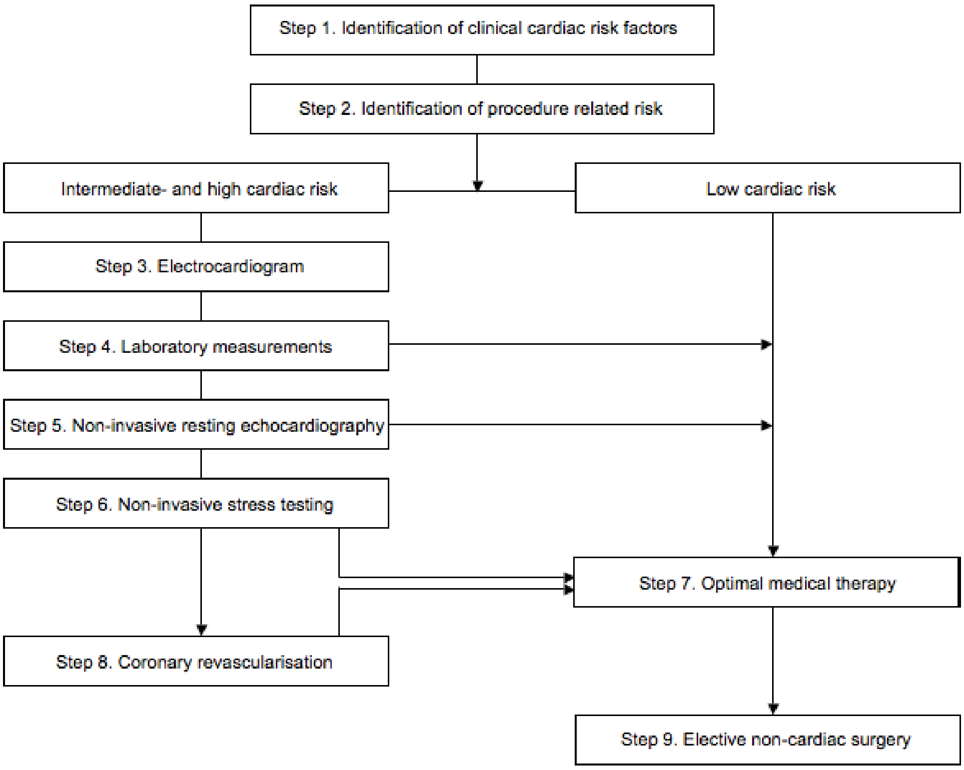
Major
• Unstable coronary syndromes
• Acute or recent myocardial infarction with evidence of important ischaemic risk by clinical symptoms or non-invasive study*
• Unstable or severe angina (Canadian class III or IV)
• Decompensated heart failure
• Significant arrhythmias
• High-grade atrioventricular block
• Symptomatic ventricular arrhythmias in the presence of underlying heart disease
• Supraventricular tachycardia with uncontrolled ventricular rate
• Severe valvular disease
Intermediate
• Mild angina pectoris (Canadian Class I or II)
• Previous myocardial infarction - by history or pathological Q waves
• Compensated or prior heart failure
• Diabetes mellitus (particularly insulin dependent)
• Renal insufficiency
Low
• Advanced age (>70)
• Abnormal electrocardiogram (left ventricular hypertrophy, left bundle-branch block, ST-T segment abnormalities)
• Rhythm other than sinus (for example atrial fibrillation)
• Low functional capacity
• History of stroke
• Uncontrolled systemic hypertension
**Recent myocardial infarction defined as > 7 days and ≤ 1 month*

Table 2

Cardiac risk stratification for non-cardiac procedures (combined risk of cardiac death and non-fatal myocardial infarction)

High
• Emergency major operations, particularly in the elderly
• Aortic and other major vascular surgery
• Peripheral vascular surgery
• Anticipated prolonged surgical procedures associated with large fluid shifts
Intermediate
• Carotid endarterectomy
• Head and neck surgery
• Intraperitoneal and intrathoracic surgery
• Orthopaedic surgery
• Prostate surgery
Low
• Endoscopic procedures
• Superficial procedures
• Cataract surgery
• Breast Surgery
High: reported cardiac risk >5%, intermediate: reported cardiac risk <5%, low: reported cardiac risk <1%

Figure 1



Cardiac risk stratification and optimisation of surgical patients

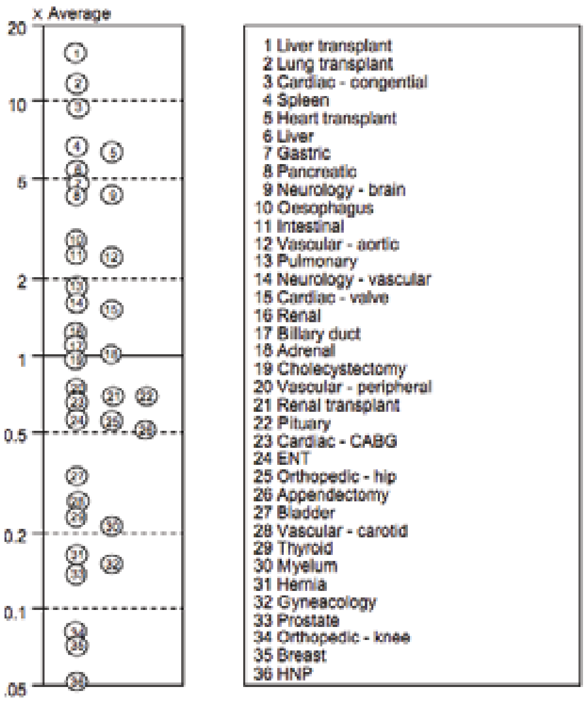
Table 3

Relationship between age and peri-operative cardiovascular death [3]

Age (yr)	Number of procedures	Number (%) of cardiovascular deaths	Odds Ratio (95% CI)
³80	5 314	77 (1.5)	19.9 (12.8-31.1)
70-80	12 619	165 (1.3)	12.6 (8.3-19.0)
60-70	15 742	146 (0.9)	8.5 (5.6-12.9)
50-60	15 675	91 (0.6)	5.6 (3.6-8.7)
40-50	16 987	37 (0.2)	2.5 (1.5-4.1)
<40	42 256	27 (0.1)	1

In the general non-cardiac surgical population, few procedure-specific data are available regarding peri-operative mortality. In fact, surgery-specific mortality has primarily been described in selected patient populations undergoing specific categories of procedures. As a result, various high risk surgical groups have been identified, with mortality rates ranging from 1.5% to 17% in major non-cardiac procedures [4, 5]. Reports of postoperative mortality in the unselected, general surgical populations are scarce. Recently, a population dataset covering a 15-yr surgical period in the general Dutch surgical population was analysed. After adjustment for differences in distribution of demographic characteristics and co-morbidities, a >256-fold difference in the incidence of postoperative mortality between the highest and lowest risk categories was noted (Figure 2). It is likely that with incorporation of surgery-specific risk classification, the predictive ability of risk stratification models will improve, resulting in more detailed information for patient and specialist.

Figure 2

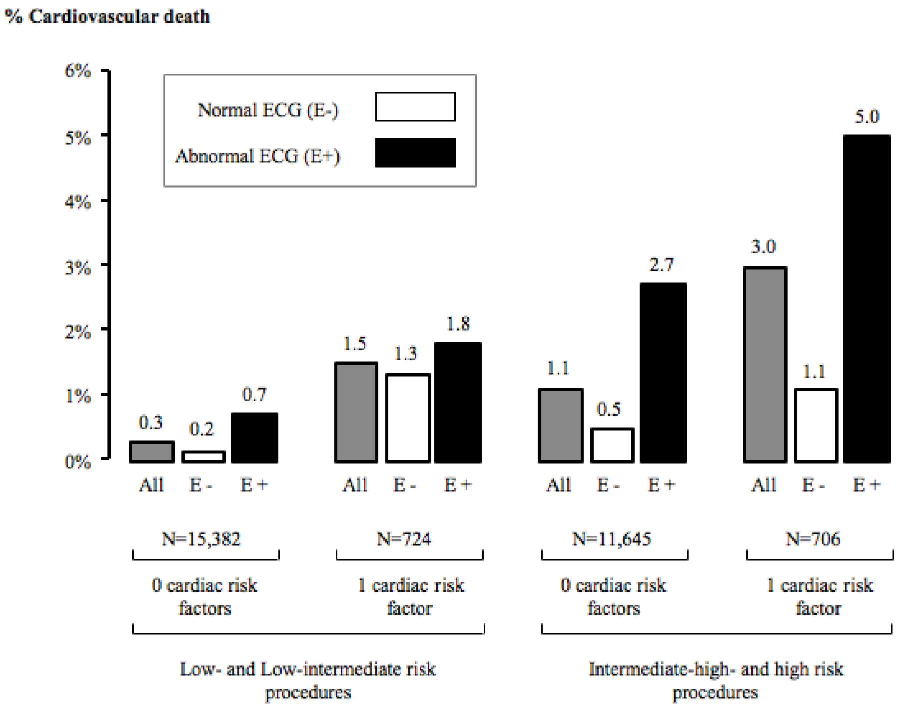


Relative mortality in sub-categories of surgical procedures

Pre-operative electrocardiography

In addition to patient characteristics and surgery related risk, pre-operative non-invasive tests are used to identify the presence and extend of CAD in patients undergoing non-cardiac surgery. In this respect, pre-operative ECG is requested in 26% of patients scheduled for non-cardiac surgery. In a study of 23 036 patients undergoing non-cardiac surgery, addition of a simple classification of the pre-operative ECG into normal or abnormal (atrial fibrillation, left or right bundle branch block, left ventricular hypertrophy, premature ventricular complexes, pacemaker rhythm, Q wave, or ST-segment changes) improved the predictive value to determine cardiovascular death during surgery [6]. Although ECG's added extra information on peri-operative cardiac risk, the increase in predictive value was small in patients undergoing lower risk procedures (Figure 3). Clinical cardiac risk markers combined with ECG and the risk of the planned surgical procedure can effectively divide patients into low-risk, intermediate-risk, and high-risk populations. In elderly patients cardiac disease is common and may be difficult to diagnose because of a lack of typical symptoms compared with younger patients. In this respect, routine ECG testing in older patients undergoing non-cardiac surgery seems justified.

Figure 3

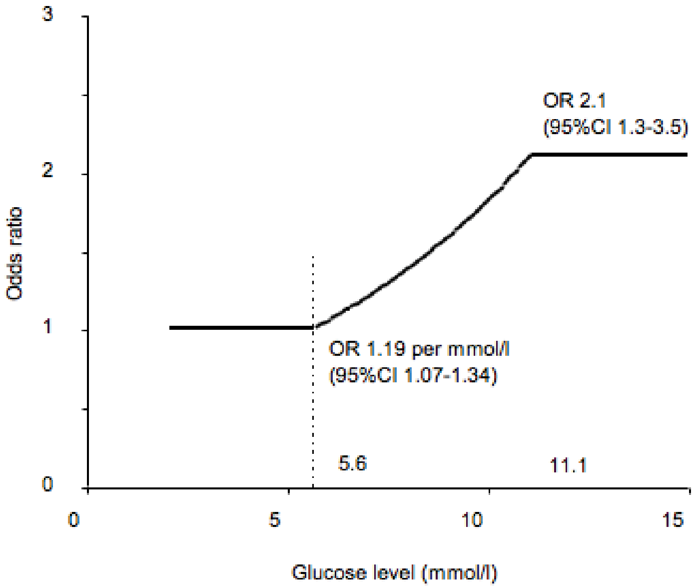


Incidence of peri-operative cardiovascular death in subgroups of patients according to type of surgery, number of cardiac risk factors and pre-operative electrocardiogram results

Pre-operative laboratory testing

Diabetes mellitus is strongly associated with older age, a combination which increases the prevalence and severity of cardiovascular disease. Pre-operative glucose testing is used to screen for asymptomatic type 2 diabetes in patients at risk for the disease. The relationship between diabetes and cardiovascular disease is assumed to begin early in the progression from normal glucose tolerance to pre-diabetes. Recently, in a case-control study of surgical patients (median age 65 years), the relationship between random pre-operative glucose levels and peri-operative mortality was analyzed [7]. Pre-diabetes glucose levels (random glucose levels > 5.6 mmo.l) in patients without a history of diabetes were associated with increased peri-operative (cardiovascular) death (Figure 4). The pre-operative metabolic state, as measured by random blood glucose measurements, identified patients at risk for peri-operative cardiovascular events. As it seems to become increasingly clear that impaired glucose metabolism and the pre-diabetes state are associated with adverse clinical outcomes, patients with pre-operative pre-diabetic glucose levels should be further screened for associated cardiovascular risk factors.

Figure 4



Relation between glucose level and relative risk for peri-operative mortality

Non-invasive cardiac imaging

Pre-operative cardiac exercise or pharmacological stress testing is recommended for patients with three or more clinical risk factors and poor functional capacity who require vascular surgery and may be considered for patients with at least one to two clinical risk factors and poor functional capacity who require intermediate-risk non-cardiac surgery, if it changes management [8]. In elderly patients the sensitivity of non-invasive cardiac stress testing increases with age, due to the higher prevalence and greater severity of coronary disease in this patient group. Patients with CAD or at risk for CAD can be frequently found in the group of patients with limited everyday exercise. In these patients pharmacological stress echocardiography or nuclear imaging are elegant ways to exclude subclinical CAD. However, stress testing should not be performed in asymptomatic patients without evidence of CAD, patients with severe co-morbidity likely to limit the life expectancy or candidacy for revascularisation, or patients with resting ECG abnormalities that preclude adequate assessment.

Reducing cardiac risk

Peri-operative pharmaceutical therapy is a non-invasive strategy to protect the heart during surgery, and possibly prevent cardiac complications. Most of the trials on medical therapy during non-cardiac surgery focus on peri-operative beta-blocker and statin therapy in intermediate or higher risk surgery. Studies of the possible protective effects of such therapies in a selected group of elderly patients are scarce.

Peri-operative beta-blockade

Slowing the heart during surgery reduces myocardial oxygen demand. It is hypothesised that due to this reduction in oxygen consumption, the coronary blood flow through pre-stenotic vessels remains sufficient enough to prevent myocardial ischaemia. Mangano and colleagues were among the first to describe the effects of peri-operative beta-blockade in a randomised controlled trial (RCT) of 200 surgical patients, with or at risk for CAD [9]. Sixty six percent of the study population was aged > 65 yr. Patients who received atenolol for one week after surgery showed a significant reduction in the rate of cardiac events during the following two years (27% vs 32%, p = 0.008) compared with those receiving placebo. However, events were counted after patients survived hospital discharge and an intention-treat analysis did not show a long-term mortality benefit.

In 1999, Poldermans and colleagues presented the results of an RCT of vascular surgical high-risk patients with reversible myocardial ischaemia on pre-operative dobutamine echocardiography [10]. All patients were aged > 60 yr. Patients treated with bisoprolol peri-operatively showed a 100% reduction in myocardial infarctions and an 80% reduction in cardiac deaths, compared with placebo treatment. The trial was stopped at the first interim analysis after randomizing 112 patients, in which a total of 20 events had occurred.

Since then many investigators have studied the effects of beta-blocker therapy and peri-operative outcome. However, several of these studies were unable to confirm the beneficial effect of peri-operative beta-blocker use on cardiovascular outcome. As a result, recent meta-analyses showed only a trend towards protection of peri-operative beta-blocker use, which was reflected in a class IIa recommendation of peri-operative beta-blocker use in patients with cardiac disease scheduled for vascular surgery and a class IIb recommendation in patients scheduled for vascular surgery without risk factors or intermediate risk surgery with the presence of one or more risk factors. Patients found to have myocardial ischaemia on pre-operative testing remained a class Ib recommendation [11].

A large RCT was set up by Devereaux and colleagues to end the ongoing debate on the protective effects of peri-operative beta-blocker therapy. The POISE (PeriOperative Ischemic Evaluation) trial randomly assigned 8 351 patients from 190 hospitals in 23 countries to either controlled release oral metoprolol succinate or placebo [12]. Patients on metoprolol showed a reduction in peri-operative cardiac events compared with placebo (combined primary endpoints cardiac death, non-fatal myocardial infarction, or cardiac arrest 5.8% vs 6.9%, odds ratio (OR) 0.84 and 95% confidence interval (CI) 0.70-0.99, p = 0.04). These results were mainly due to a reduction in non-fatal myocardial infarction (4.2% vs 5.7%, OR 0.73 and 95% CI 0.60-0.89, p = 0.002). However, the benefit in peri-operative cardiovascular outcome was associated with an increased incidence of all-cause mortality (3.1% vs 2.3%, OR 1.33 and 95% CI 1.03-1.74, p = 0.03) and stroke (1.0% vs 0.5%, OR 2.17 and 96% CI 1.26-3.74, p = 0.005). Stroke was associated with peri-operative hypertension, bleeding, atrial fibrillation and a history of stroke or transient ischaemic attack in patients assigned to metoprolol. Age > 70 yr was an independent predictor of death (OR 1.65 and 95% CI 1.20-2.26). Thus, the POISE trail showed evidence of cardiac protection at the cost of an increased incidence of peri-operative stroke and all-cause mortality.

Several issues regarding the conflicting evidence for peri-operative beta-blocker use need to be resolved in future research, for example the initiation time and dosing of beta-blocker therapy, the type of beta-blocker and dose adjustments for heart rate control. The recommendation that patients already on beta-blockers continue their medication throughout the peri-operative period remains, as POISE only studied the effects on outcome of acute peri-operative beta-blockade and the withdrawal of beta-blockers before surgery has been associated with an increased incidence of adverse events.

Peri-operative statin therapy

A considerable proportion of the surgical population is believed to have undiagnosed, asymptomatic CAD, characterised by non-blood flow limiting, vulnerable atherosclerotic plaques. Recent studies have suggested that as a result of the anti-inflammatory action and reversal of endothelial dysfunction peri-operative statin therapy is associated with improved cardiac outcome of high-risk non-cardiac surgical patients [13, 14]. However, the possible protective effect of statins in the general surgical population is not known and studies in the elderly population are lacking. Although the studies published so far are in favour of peri-operative statin treatment, this needs to be confirmed in large, adequately powered randomised trials.

Pre-operative revascularisation

Recent findings of the Coronary Artery Revascularization Prophylaxis Trial showed no survival benefit of pre-operative coronary revascularisation in cardiac stable patients scheduled for elective vascular operations with evidence of severe coronary stenosis at coronary angiography [15]. Anatomical criteria of exclusion included > 50% stenosis of the left main coronary artery, left ventricular ejection fraction < 20%, and severe stenosis of the aorta. Patients were randomised either to optimal medical treatment (more than 80% were on ß-blocker therapy in both groups) with or without coronary revascularisation or to percutaneous coronary intervention (59%, mean 18 days before surgery) or coronary artery bypass graft surgery (41%, mean 54 days before surgery). No differences in mortality in long-term outcome (median follow-up 2.7 yr) were found: 22% and 23% in the revascularisation and non-revascularisation groups, respectively. Although the primary end point was late mortality, even the findings at 30 days did not show any difference in terms of mortality or postoperative myocardial infarction, nor did ‘prophylactic’ revascularisation result in a reduction of the length of hospital stay.

Conclusion

Elderly patients undergoing major non-cardiac surgical procedures are at increased risk for complications during the surgical period due to an increased prevalence of (asymptomatic) CAD and subsequent risk of peri-operative cardiac complications. Patient characteristics, type of surgery and pre-operative ECG can effectively divide patients into a low-risk, intermediate-risk, and high-risk population. Low-risk patients should proceed with surgery as additional cardiac testing is unlikely to alter peri-operative management. Intermediate-risk patients may be referred for cardiac testing to exclude extensive stress induced myocardial ischaemia, but only if it changes peri-operative management. Whether patients at intermediate risk without ischaemic heart disease should be treated with statins and/or beta-blockers is still subject of debate. Beta-blockers are recommended in patients with ischaemic heart disease and should be continued in patients on chronic beta-blocker treatment. The optimal peri-operative evaluation and management of patients with multiple risk factors and extensive stress-induced ischaemia remains controversial. Success will depend on careful collaboration between cardiologists, anaesthesiologists, and surgeons.

Key Learning Points

- Advanced age is an independent predictor of peri-operative cardiac mortality.
- Patient characteristics, type of surgery and pre-operative ECG can effectively differentiate between low and high risk older surgical patients.
- Low risk surgical patients should proceed with surgery as additional cardiac testing is unlikely to alter peri-operative management.
- Beta-blockers are recommended in patients with ischaemic heart disease and should be continued in patients on chronic beta-blocker treatment.

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