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### **Review** article

# Dual antiplatelet therapy in patients with acute coronary syndrome treated by surgical revascularization



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#### ABSTRACT

Twelve months dual antiplatelet therapy (DAPT) based on a combination of acetylsalicylic acid and purine receptor P2Y12 inhibitor is a standard for all patients with acute coronary syndrome (unstable angina pectoris, NSTEMI and STEMI). Previous sub-analysis of CURE and ACUITY studies suggested that DAPT could bring benefit even for patients treated by surgical revascularization. Sub-analysis of PLATO trial conducted on 1261 patients, who underwent surgical revascularization within 12 months, demonstrated a reduction of cardiovascular and total mortality within a group of patients treated by ticagrelor and acetylsalicylic acid compared to patients treated by clopidogrel and acetylsalicylic acid.

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#### Introduction

According to current ESC guidelines for the management of acute coronary syndrome in patients presenting with or without ST-segment elevation, patients should undergo 12 months of dual antiplatelet therapy (DAPT) after the myocardial infarction irrespective of whether they are treated with percutaneous coronary intervention or conservatively, with pharmacotherapy only [1,2]. Part of the patients hospitalized due to acute coronary syndrome (ACS) are treated with a coronary artery bypass graft (CABG) in the acute stage, electively after discharge or later because of progression of atherosclerosis or development of in-stent restenosis. The number of patients treated with invasive strategy at a higher age is growing along with the improved care for patients with ACS. According to the Euroheart ACS 2001 survey of patients who underwent coronary angiography for ACS suspicion, a total of 35.2% of men and 29.8% of women aged 55-64 years, 38.8% of men and 34.1% of women aged 65-74 years, and 46.6% of men and 40.1% of women aged over 75 years had a three-vessel disease [3]. Table 1 illustrates the growing portion of invasively examined patients with ACS between 1999 and 2008 (from 43% up to 85%); increasing proportion of patients were treated with percutaneous coronary intervention (PCI) (from 21% up to 64%), while the number of patients treated with surgical revascularization remains stable and moves around 11%.

The question remains whether a patient after ACS in whom significant and unstable atherosclerotic lesions were bridged by CABG (arterial or venous) is stable and should be treated similarly as a patient after surgical revascularization for the stable form of coronary artery disease (CAD), or whether he

Table 1 – Part of patients with acute coronary syndrome in studies and registers who were examined invasively and treated by percutaneous coronary intervention (PCI) and surgical revascularization (CABG) between 1999 and 2008.

	Coronary angiography	PCI	CABG	
CURE (1999) [13]	43.7%	21.2%	16.5%	
EHS-ACS I (2000) [3]	52.0%	25.4%	5.4%	
GRACE registry (2000) [14]	53%	28%	10%	
EHS-ACS II (2004) [15]	62.9%	37.1%	7.4%	
CZECH registry (2005) [16]	85%	54%	12%	
PLATO (STEMI and NSTEMI) (2008) [17]	81.4%	64.1%	10.2%	
PCI, percutaneous coronary intervention; CABG, coronary artery				

bypass graft.

still remains a patient after ACS with the presence of an unstable atherosclerotic plaque and should be treated with dual antiplatelet therapy for 12 months after the onset of ACS.

# Antiplatelet therapy for patients post-CABG with a stable form of CAD

According to ACCF/AHA guidelines, patients with a stable form of CAD post-CABG revascularization should be treated with acetylsalicylic acid (ASA) in a dose of 100–325 mg, which should be administered perioperatively or as soon as the patient's bleeding is stabilized - ideally 6 h after the surgery and after 48 h at the latest. Clopidogrel is the alternative in the case of ASA intolerance. This treatment lowers the risk of venous graft closure. Warfarin did not turn out to be as effective [4]. Two smaller recent studies demonstrated that DAPT based on the combination of ASA with clopidogrel could also be beneficial for such stable patients after CABG. López et al. reported in a group of 237 patients treated by CABG offpump that during 24-month follow-up, rehospitalization for ACS decreased (10.9% vs. 3.7%, p = 0.035), and combined endpoint occurrence decreased as well (ACS, revascularization, stroke and cardiovascular deaths; 18.8% vs. 8.3%; p = 0.02) with dual antiplatelet therapy [5]. Gao at el. have demonstrated lower risk of venous graft closure after three months of DAPT with ASA plus clopidogrel compared to ASA itself (91.6% vs. 85.7%, p = 0.043) [6].

#### Dual antiplatelet treatment with clopidogrel together with ASA after CABG in CURE and ACUITY studies in ACS patients

Comparison of dual antiplatelet therapy with the combination of ASA plus clopidogrel vs. ASA itself in ACS patients presented without ST elevation was evaluated in the CURE study (clopidogrel in unstable angina pectoris to prevent recurrent ischemic events). Out of the total of 12,562 patients, 2072 underwent surgical revascularization during the course of the study. The sub-analysis results were consistent with the results of the entire study; the occurrence of combined primary end-point (cardiovascular deaths, MI or stroke) was lower in the group of patients treated with DAPT; however, without reaching statistical significance (14.5% vs. 16.2%; RR = 0.98; 95% CI 0.71-1.11). The outcome was similar in patients treated both in the early stage of ACS and during the entire course of the study. The positive effect of DAPT was seen especially during the period prior to surgical revascularization. After surgery, the median of DAPT interruption (study medication) was 10 days and DAPT was initiated again in 75.3% of the patients. The occurrence of cardiovascular events

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