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Initiation and duration of dual antiplatelet therapy after inpatient percutaneous coronary intervention with stent implantation in Germany: An electronic healthcare database cohort study

Initiierung und Dauer der dualen Thrombozytenaggregationshemmung nach stationärer perkutaner koronarer Intervention mit Stentimplantation in Deutschland: eine Kohortenstudie auf der Grundlage von Abrechnungsdaten

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ABSTRACT

Background: Studies assessing the routine outpatient dual antiplatelet therapy (DAPT) after percutaneous coronary intervention (PCI) in Germany are scarce. The aim of this study was (i) to investigate the initiation and duration of DAPT after inpatient PCI with stent implantation in Germany, and (ii) to identify factors associated with DAPT discontinuation during the recommended treatment period.
Methods: This retrospective cohort study was based on data from a large German electronic healthcare database of the years 2004 to 2009. The study population comprised four groups of patients with acute coronary syndrome (ACS) or stable angina pectoris undergoing inpatient PCI with either bare metal stent (BMS) or drug eluting stent (DES) implantation between 2005 and 2008. Initiation of outpatient DAPT within a period from 100 days before the PCI to 60 days after the PCI was ascertained. Time until end of treatment was analysed using the Kaplan-Meier method. Factors potentially associated with DAPT discontinuation, like sex, age, cardiovascular comorbidity, contraindications, and other antithrombotic drugs were analysed in a Cox proportional hazard model.
Results: The cohort comprised 37,001 patients. Depending on the type of stent and the indication for the PCI, DAPT was initiated in 85 % (ACS/BMS) and 95 % (AP/DES) of all patients. Of those, 12 % (AP/DES) and 64 % (ACS/BMS) discontinued DAPT during the recommended treatment duration. An age of over 80 years (OR 1.2–1.5 compared to patients aged 0-49 years) and the use of phenprocoumon (OR 2.7–5.0 compared to no phenprocoumon) were associated with an increased risk of DAPT discontinuation.

Abbreviations: ACS, Acute coronary syndrome; AP, Angina pectoris; ASA, Acetylsalicylic acid; ATC, Anatomical-therapeutical-chemical classification; BMS, Bare metal stent; CAD, Coronary artery disease; DAPT, Dual antiplatelet therapy; DDD, Defined daily dose; DES, Drug eluting stent; ESC, European Society of Cardiology; GePaRD, German Pharmacoepidemiological Research Database; PCI, Percutaneous coronary intervention; SHI, Statutory health insurance; VKA, Vitamin K antagonists.

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Conclusions: A high proportion of patients with coronary artery disease undergoing inpatient PCI with stent implantation received DAPT. However, DAPT discontinuation during the recommended time span was frequent, particularly in patients suffering from ACS. On the other hand, especially patients with AP and DES were often treated longer than recommended.

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ZUSAMMENFASSUNG

Hintergrund: Studien, in denen der ambulante Einsatz der dualen Thrombozytenaggregationshemmung (DTAH) nach einer stationären perkutanen koronaren Intervention (PCI) im klinischen Alltag bewertet wird, sind in Deutschland selten. Ziel dieser Studie war es, die Initiierung und die Dauer der DTAH nach stationärer PCI mit Stentimplantation in Deutschland zu untersuchen und Faktoren zu identifizieren, die mit einem Abbruch der DTAH im empfohlenen Therapiezeitraum assoziiert waren.
Methodik: Diese retrospektive Kohortenstudie basiert auf Routinedaten der gesetzlichen Krankenversicherung aus den Jahren 2004 bis 2009. Die Studienpopulation bestand aus vier Gruppen von Patienten mit akutem Koronarsyndrom (ACS) bzw. stabiler Angina pectoris (AP), die sich zwischen 2005 und 2008 einer stationären PCI mit Implantation eines „bare metal stent" (BMS) oder eines „drug eluting stent" (DES) unterzogen. Die Initiierung der ambulanten DTAH wurde innerhalb von 100 Tagen vor und 60 Tagen nach PCI bestimmt. Die Zeit bis zum Abbruch der Therapie wurde mittels Kaplan-Meier-Methode bestimmt. In einem Cox-Regressionsmodell wurde der Einfluss von Geschlecht, Alter, kardiovaskulärer Komorbidität, Kontraindikationen und anderen antithrombotischen Medikamenten auf die Wahrscheinlichkeit eines Therapieabbruchs untersucht.
Ergebnisse: Die Kohorte bestand aus 37.001 Patienten. Je nach Stenttyp und Indikation für die PCI wurde die DTAH in 85 % (ACS/BMS) bzw. 95 % (AP/DES) aller Patienten initiiert. Von diesen beendeten 12 % (ACS/BMS) bzw. 64% (AP/DES) die DTAH noch während des empfohlenen Zeitraums. Ein Alter über 80 Jahren (OR 1,2–1,5 verglichen mit 0- bis 49-jährigen Patienten) und der Gebrauch von Phenprocoumon (OR 2,7–5,0 verglichen mit Patienten ohne Phenprocoumon) waren mit einem erhöhten Risiko für einen Abbruch der DTAH assoziiert.
Schlussfolgerungen: Ein großer Anteil von Patienten erhält nach einer PCI mit Stentimplantation eine DTAH. Dennoch konnte häufig ein Abbruch der DTAH innerhalb des empfohlenen Zeitraums beobachtet werden, besonders bei Patienten mit einem ACS. Auf der anderen Seite werden besonders Patienten mit AP und DES häufiger länger behandelt, als in der Leitlinie empfohlen.

Introduction

Coronary artery disease (CAD) is the most common cause of death in industrialized countries. In 2012, 15% of all deaths occured due to CAD in Germany [1]. The lifetime prevalence of CAD in German individuals aged 65 years or older is 15% and increases with advancing age [2]. Percutaneous coronary interventions (PCIs) are increasingly used in the therapy of CAD. Over the last decade, the number of PCIs in Germany rose from 180,000 in 2000 to over 335,000 in 2010 with an increasing proportion of PCIs with implantation of bare metal stents (BMS) or drug eluting stents (DES) [3–5]. To prevent stent thrombosis after PCI, dual antiplatelet therapy (DAPT) is recommended. This comprises lifelong acetylsalicylic acid (ASA) and a thienopyridine (e.g. clopidogrel or, less commonly, ticlopidine) for a limited period of time [6]. The duration of DAPT currently recommended by the European Society of Cardiology (ESC) depends on the type of stent and the indication for the PCI. In patients with acute coronary syndrome (ACS), DAPT should be given for a period of twelve months after the intervention, independently of the type of the stent. The recommended duration of DAPT after PCI in patients with stable angina pectoris (AP) is one month for BMS and six months for DES. However, during the whole study period the ESC-guideline published in 2005 was valid. The recommendations differed only for patients with ACS, who should get DAPT nine to twelve months instead of twelve months generally. The recommended duration of DAPT after PCI in patients with AP was still one month for BMS and six months for DES [7].

These recommendations are based on the observation that DAPT reduces major adverse cardiac events after PCI in patients with both stable angina and ACS as compared with ASA alone, or ASA in combination with a vitamin-K-antagonist [8]. Treatment with DAPT after PCI with stent implantation is critical to prevent early and late stent thrombosis and in-stent restenosis, which may be caused via intravascular clot formation or intimal hyperplasia on the surface of the stent [9,10]. DAPT discontinuation in the first 30 days after DES implantation was associated with an 8-fold increased risk of stent thrombosis compared to patients without therapy discontinuation [11].

In Germany, only few studies have assessed drug treatment after PCI. These studies were either conducted before the publication of current guidelines [12], only covered drug treatment in the inpatient setting [13], or were limited to a small and regional sample [14].

Up to date evidence from health care services research on medical treatment of patients undergoing PCI is essential to evaluate the adequacy of drug treatment, particularly in the context of an aging society and the associated increasing numbers of patients suffering from CAD.

The aims of this study were to (i) investigate the initiation and duration of outpatient DAPT in patients with ACS or stable AP, undergoing inpatient PCI with stent implantation in Germany and (ii) to identify factors associated with the discontinuation of DAPT.

Methods

Data source

This study was based on data from the German Pharmacoepidemiological Research Database (GePaRD). GePaRD currently comprises claims data from four statutory health insurances (SHIs) including data of more than 20 million insurants. The database has