Canadian Journal of Cardiology 35 (2019) 931–934

Training/Practice
Health Policy and Promotion

Factors Affecting Delay in Filling Prescriptions for Dual Antiplatelet Therapy After Coronary Stenting

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ABSTRACT

Dual antiplatelet therapy (DAPT) is critical in preventing stent thrombosis after percutaneous coronary intervention (PCI). Delays in DAPT after PCI have been associated with stent thrombosis, reinfarction, and death. Cases of death, stent thrombosis, and reinfarction at our institution have been attributed to patient delays in accessing DAPT on discharge after PCI. We sought to determine the proportion of patients that delay filling their discharge prescription for DAPT after PCI and factors that influence delays in DAPT prescription-filling. We reviewed all patients who received PCI at St Paul's Hospital from April 1, 2015 to April 1, 2016 and determined the date of the first prescription filling of a P2Y12 antiplatelet agent after hospital discharge. The primary outcome was proportion of patients who delay filling their DAPT discharge prescription. Logistic regression analysis was performed to

RÉSUMÉ

La bithérapie antiplaquettaire joue un rôle crucial dans la prévention de la thrombose de l'endoprothèse après une intervention coronarienne percutanée (ICP). Le recours tardif à la bitherapie antiplaquettaire après une ICP a été associé à la thrombose de l'endoprothèse, à un nouvel infarctus et au décès. Des cas de décès, de thrombose de l'endoprothèse et de nouvel infarctus survenus dans notre établissement ont été attribués au fait que le patient avait tardé à commencer une bitherapie antiplaquettaire après avoir quitté l'hôpital où il avait subi une ICP. Nous avons voulu savoir quelle est la proportion des patients qui tardent à faire exécuter leur ordonnance de bitherapie antiplaquettaire après une ICP et quels sont les facteurs qui influent sur un tel retard. Nous avons examiné les dossiers de tous les patients ayant subi une ICP à l'hôpital St. Paul entre le 1er avril 2015 et

Percutaneous coronary intervention (PCI) with coronary artery stent insertion is a common procedure in patients with stable angina and acute coronary syndromes. A major complication of PCI is stent thrombosis and is estimated to occur in approximately 1% of patients.[1] Although the incidence of stent thrombosis is low, the mortality associated with this complication is 25%-50% and patients commonly present with ST-elevation myocardial infarction (MI). Stent thrombosis is associated with significant morbidity among survivors, as well.[2] The universally accepted therapy for prevention of stent thrombosis is dual antiplatelet therapy (DAPT), consisting of acetylsalicylic acid taken in combination with a P2Y12 antagonist such as clopidogrel, prasugrel, or ticagrelor.[3]

The importance of patients' adherence to DAPT after PCI and coronary artery stent insertion in preventing stent thrombosis is strongly emphasized in cardiology guidelines.[3] DAPT must be continued for a minimum of 1 month in patients with a bare metal coronary stent and at least 1 year (and up to 3 years) in those who received a drug-eluting coronary stent. Standard of care also includes educating patients on the importance of adherence to DAPT and strong encouragement to fill their prescription for DAPT immediately after hospital discharge.

Previous research has estimated that 30% of PCI patients fail to fill their DAPT prescription within 3 days of hospital discharge.[4] In another study, researchers showed that 16% of patients did not fill their prescription for DAPT on the day of

Received for publication January 25, 2019. Accepted March 31, 2019.

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See page 934 for disclosure information.

https://doi.org/10.1016/j.cjca.2019.03.025

determine the relationship of various factors with delays in DAPT-filling. Six hundred fifty-one patients were included in the final analysis. Age, sex, and provincial drug coverage status were not associated with delays in DAPT prescription-filling. Distance of patient's residence to St Paul's Hospital was associated with a significant delay in DAPT prescription filling (adjusted odds ratio, 1.90; 95% confidence interval, 1.11-3.22). Hospital discharge processes to ensure timely access to DAPT after PCI should be established.

le 1er avril 2016 et avons déterminé la date de la première exécution d'une ordonnance d'agent antiplaquettaire après le congé de l'hôpital. Le paramètre d'évaluation principal était la proportion des patients tardant à faire exécuter l'ordonnance de bitherapie antiplaquettaire qui leur est remise à leur sortie de l'hôpital. Une analyse de régression logistique a été réalisée en vue de déterminer la relation entre différents facteurs et le retard à faire exécuter l'ordonnance de bitherapie antiplaquettaire. Six cent cinquante et un patients ont été inclus dans l'analyse finale. L'âge, le sexe et le fait que le médicament soit ou non remboursé par le régime public provincial n'étaient pas associés à des retards dans l'exécution de l'ordonnance de bitherapie antiplaquettaire. La distance séparant la résidence des patients de l'hôpital St. Paul était associée à un retard significatif d'exécution de l'ordonnance de bitherapie antiplaquettaire (rapport de cotes ajusté, 1,90; intervalle de confiance à 95 %, de 1,11 à 3,22). Il est recommandé d'instaurer des procédures de congé hospitalier assurant un accès rapide à la bitherapie antiplaquettaire après une ICP.

discharge, with the median delay being 3 days, which was associated with increased mortality and MI rates.[5] Importantly, delays in DAPT therapy, even as short as 1 day, are associated with a twofold increase in risk of mortality and recurrent MI.[5]

Canadian PCI centres are located in major cities; therefore, patients who require PCI but do not live in a major urban centre have to travel or be transported for their procedure. St Paul's Hospital (SPH), in Vancouver, British Columbia (BC) is the quaternary cardiac referral centre for the province of BC and Yukon and performs a high volume of PCI procedures, serving patients from across the province. In fact, most patients who undergo PCI at SPH reside outside the city of Vancouver and travel distances ranging from 50 to more than 2000 km for their procedure, with journeys sometimes in excess of 1 full day.

Recent cases of stent thrombosis at SPH (resulting in death, reinfarction, and rehospitalization) have been attributed to patients not filling or delaying filling their DAPT prescription. This prompted our study to determine what proportion of PCI patients delay filling their DAPT prescription and what demographic and geographic factors influence delay in DAPT prescription-filling.

Methods

Our study received approval from the University of British Columbia/Providence Health Care Research Ethics Board (H16-02764) and from the BC Ministry of Health, Information Management and Knowledge Services Branch, Health Sector Information Analysis and Reporting Division. This was a single-centre, retrospective, observational study of all patients who received PCI with coronary artery stenting at SPH between April 1, 2015 and April 30, 2016. Patients were excluded if they died during their PCI hospitalization, lived outside of BC, were transferred to another hospital facility, were receiving DAPT before PCI, or had no prescription records on PharmaNet. PharmaNet is the BC drug database for all outpatient prescriptions filled at a community pharmacy in the province by BC residents and all provincial drug coverage plans are administered through this database. A list of the Personal Health Numbers of patients who met the inclusion criteria was obtained from SPH health records, as well as date of hospital discharge, demographic data, and the local health region of the patient's residence. Using this extract, we obtained a linkage with BC provincial outpatient prescription records (PharmaNet) for the date of first filling of any DAPT prescription (clopidogrel, prasugrel, or ticagrelor) after discharge from hospital, within the study period.

The primary outcome was the proportion of patients who delayed filling their DAPT prescription (defined as $>$ 1 calendar day after hospital discharge date). Secondary outcomes evaluated included the association of delay in prescription-filling of DAPT with distance from hospital, sex, age, and provincial drug coverage plan.

Demographic variables (age, sex, and distance of residence from the hospital), were summarized with descriptive statistics. We dichotomized distance of residence from the hospital as "distant" (locations that required $>$ 2 hours' travel by car, as estimated by Google Maps, or any ferry trip, which would often mean arriving home after local pharmacies have closed) or "near" (less than 2 hours' travel by car). Predictors of delay were modelled using multivariate logistic regression and controlling for age, sex, drug coverage, and distance from PCI centre using SPSS version 25.0 (IBM Corp, Armonk, NY). We calculated DAPT prescription-filling time as the difference in date (days) between discharge date and first prescription filling date of DAPT within the study time frame.

Results

One thousand forty-eight patients who underwent PCI at SPH between April 1, 2015 and March 31, 2016 were identified. Three hundred ninety-seven patients were excluded, resulting in a final sample of 651 patients (Fig. 1). The mean age of patients was 65 years and most (75%) were male. Forty-four percent of patients lived near SPH whereas 55% lived distant to SPH. Most of the patients (84%) filled the prescription within 24 hours after discharge, 90% of patients filled their DAPT prescriptions within 48 hours, with 93% filling within 72 hours. The antiplatelet agents prescribed were as follows; clopidogrel 56%, prasugrel 3%, and ticagrelor 41%.

There were no age or sex differences between patients who filled their discharge DAPT prescription on time and those who delayed (Table 1). There was also no difference in

timeliness of filling between those with social assistance provincial drug coverage plan (no cost to the patient) compared with patients with income-based drug coverage (co-payment required). However, a higher proportion of patients who lived distant to SPH delayed DAPT prescription-filling compared with those living near. In multivariate analysis, only distance from PCI centre remained a significant predictor of delayed DAPT filling.

Discussion

In this retrospective study, age, sex, and drug coverage did not influence timely filling of DAPT prescriptions, but distance of residence from PCI hospital did. This is contrary to previous studies that have suggested that age is a factor in delayed prescription-filling.[5] As well, 84% of the patients in our study filled their prescription within 24 hours of hospital discharge, which is higher than previously reported in other studies.[4,5] We postulated that having income-based drug insurance coverage might be a proxy for patients' social-economic status. However, our results indicated that insurance coverage did not influence timely DAPT prescription-filling. Our findings are unique, showing a nonclinical factor is associated with delays in DAPT prescription filling. Living distant from a PCI centre poses multiple logistical barriers to patients on discharge. Relevant to DAPT are arranging transportation home and obtaining discharge medications from a community pharmacy in a timely manner. Transportation home can be complex, potentially involving flights, bus transfers, or ferries. Thus, the complexity of transportation home could influence timely filling of DAPT prescription. Although our definition of living distant from a PCI centre of transportation time > 2 hours is arbitrary, it illustrates that patients who do not live within an accessible distance from a PCI centre are more likely to delay filling their discharge prescription.

We recommend that hospital discharge processes to aid in prompt access to DAPT therapy on discharge should be established for patients who live distant from PCI hospitals. For example, delays could be minimized by the hospital providing an interim supply of DAPT. Some hospitals have implemented this and other processes, such as telephone follow-up after discharge to ensure DAPT therapy is continued, or close collaboration with a local community pharmacy to facilitate prompt prescription filling. These processes should be tailored to local needs and policies, but our analysis provides clear, contemporary evidence for initiating or sustaining such processes.

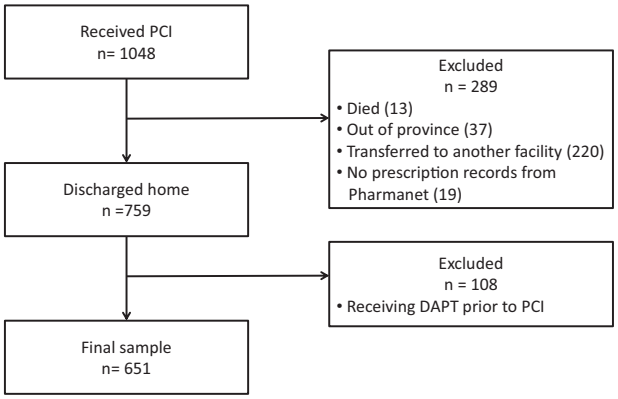

Figure 1. Derivation of study sample. DAPT, dual antiplatelet therapy; PCI, percutaneous coronary intervention.

A limitation of our study is that we did not evaluate the association of DAPT filling delay with clinical outcomes such as reinfarction, hospital readmission, stent thrombosis, or death. However, previous studies have uniformly shown that delays in obtaining DAPT prescriptions are associated with an increased rate of reinfarction, hospital readmission, and death.[5] Further limitations are that the provincial PharmaNet database only contains data on prescription-filling, not whether patients actually take the medications and that we were not able to assess other sociodemographic factors that might contribute to prescription-filling behaviour, such as education level or health literacy, because of the retrospective nature of our study.

In conclusion, age, sex, and drug coverage did not influence timing of DAPT prescription filling; however, living distant from the PCI hospital was associated with a significant delay. Hospital discharge processes (eg, providing an interim supply of DAPT) to assist patients who must travel long distances home after their PCI are needed, to ensure timely DAPT therapy.

Table 1. Association of prescription-filling delay with selected demographic factors (adjusted and unadjusted)

Variable	Prescription-filling delay		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
	No (n = 547)	Yes (n = 104)		
Distance from PCI centre, n (%)				
< 2 hours	256 (88.6)	33 (11.4)	1.46 (1.09-2.00)	1.90 (1.11-3.22)
> 2 hours	292 (80.7)	70 (19.3)		
Sex, n (%)				
Male	414 (85.0)	73 (15.0)	0.94 (0.84-1.05)	0.79 (0.43-1.47)
Female	134 (88.2)	18 (11.8)		
Mean age, years	64.9	65.0	*	1.01 (0.99-1.03)
Drug coverage				
Deductible co-payment required, n (%)				
No (social assistance)	41 (87.2)	6 (12.8)	1.06 (0.47-2.41)	1.08 (0.43-2.70)
Yes (income-based)	423 (86.5)	66 (13.5)		

No additional variables were included in the analysis.

CI, confidence interval; OR, odds ratio; PCI, percutaneous coronary intervention.

* P = not significant.

Disclosures

The authors have no conflicts or potential conflicts of interest to disclose.

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