Late outcomes following percutaneous coronary interventions: Results from a large, observational registry

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BACKGROUND: Randomized controlled trials report short- and medium-term outcomes following percutaneous coronary intervention (PCI), but their applicability to the general population is not known. Data regarding the long-term clinical outcomes of patients undergoing PCI are lacking.

OBJECTIVE: To determine the long-term outcomes of 'all-comers' undergoing PCI at a large-volume tertiary cardiac referral centre.

METHODS: A total of 12,662 consecutive patients undergoing an index procedure and entered into the University Health Network's (Toronto, Ontario) prospective registry between April 2000 and September 2007 were identified. In-hospital outcomes were assessed. Follow-up data were obtained through linkage to a provincial registry. Kaplan-Meier analysis was performed to calculate unadjusted survival rates, and Cox multiple regression analysis identified independent predictors of late mortality, major adverse cardiac events and all cardiovascular events.

RESULTS: The population included a relatively high-risk patient cohort, with 19% older than 75 years of age, 28% with diabetes, 61% with multi-vessel disease and 1.3% in cardiogenic shock. Urgent procedures comprised 53% of all cases. The all-cause mortality rate at seven years follow-up was 10.6%. Repeat PCI occurred in 14.2% of patients, and coronary artery bypass grafting in 4.2%. Men showed a significant unadjusted survival advantage compared with women. Procedural characteristics such as incomplete revascularization and residual stenosis, in addition to established risk factors, were predictors of poorer long-term outcomes. Cardiogenic shock was the strongest predictor of late mortality.

CONCLUSION: In the present large registry of 'all-comers' for PCI, long-term major adverse cardiac event rates were low and consistent with outcomes from randomized controlled trials. These data reflect a large cohort in real-world clinical practice, and may help clinicians further characterize and better treat high-risk patients who are undergoing PCI.

Key Words: *Clinical outcomes; Mortality; PCI*

The introduction of coronary stent implantation heralded a major advance in percutaneous coronary intervention (PCI), with dramatically improved in-hospital mortality and morbidity compared with plain old balloon angioplasty for the treatment of coronary artery disease. Several randomized controlled trials (RCTs) have established the superior long-term safety and efficacy of bare-metal stenting (BMS) compared with plain old balloon angioplasty (1-3). The introduction of drug-eluting stents (DES) resulted in a further significant reduction in restenosis, and has been associated with improved procedural outcomes in a more complex subset of patients and lesions (4-7). Thus, coronary stenting using bare-metal or drug-eluting platforms has become the cornerstone of PCI, and the indications for PCI have vastly expanded beyond those originally proposed.

Pooled data from randomized DES trials have shown acceptable rates of all-cause mortality, myocardial infarction (MI) and

Issue tardive des interventions coronariennes percutanées : Résultats d'un volumineux registre d'observation

HISTORIQUE : Des essais contrôlés et randomisés font état des résultats à court et à moyen terme des interventions coronariennes percutanées (ICP), mais leur applicabilité à la population générale est inconnue. On dispose de trop peu de données sur l'issue clinique à long terme chez les patients qui subissent une ICP.

OBJECTIF : Déterminer l'issue à long terme de l'ICP chez tous les patients qui y ont été soumis dans un grand centre de soins cardiaques tertiaires.

MÉTHODE : En tout, on a recensé 12 662 patients consécutifs soumis à une première intervention qui ont été inscrits au registre prospectif du Réseau universitaire de santé (Toronto, Ontario) entre avril 2000 et septembre 2007. Les auteurs ont évalué l'issue perhospitalière. Ils ont obtenu des données de suivi auprès d'un registre provincial intégré. Ils ont effectué une analyse de Kaplan-Meier pour calculer les taux de survie non ajustés et l'analyse de régression multiple de Cox a permis de dégager des prédicteurs indépendants de mortalité tardive, de complications cardiaques majeures et de complications cardiovasculaires, tous types confondus.

RÉSULTATS : La population comprenait une cohorte de patients à risque relativement élevé, dont 19 % avaient plus de 75 ans, 28 % souffraient de diabète, 61 %, de maladie plurivasculaire et 1,3 %, de choc cardiogénique. Les interventions étaient urgentes dans 53 % de tous les cas. Le taux de mortalité de toutes causes après sept ans de suivi était de 10,6 %; 14,2 % des patients ont subi une autre ICP, tandis que 4,2 % ont subi un pontage coronarien. Les hommes ont présenté un avantage significatif sur le plan de la survie non ajustée, comparativement aux femmes. Les caractéristiques des interventions, comme revascularisation incomplète et sténose résiduelle, en plus des facteurs de risque établis se sont révélées des prédicteurs d'un piètre pronostic à long terme. Le choc cardiogénique a été le plus important prédicteur de mortalité tardive.

CONCLUSIONS : Dans ce volumineux registre de tous les patients soumis à une ICP, les taux de complications cardiaques majeures à long terme ont été faibles et ont concordé avec les résultats des essais randomisés et contrôlés. Ces données sont le reflet de la pratique clinique concrète auprès d'une importante cohorte et pourraient aider les cliniciens à caractériser davantage et à traiter plus efficacement les patients à haut risque qui doivent subir une ICP.

revascularization in extended follow-up, up to four years (8). Although RCTs have excellent internal validity, direct extrapolation of their findings to the general population has been problematic due to their restrictive inclusion and exclusion criteria. Early data (9,10) regarding clinical outcomes in real-world patient reports from registries had limitations in both the follow-up period and the patient cohort size; the large New York State registry (11) comparing three-year outcomes in patients undergoing coronary stenting versus coronary artery bypass graft (CABG) surgery excluded all those with previous revascularization, left main stem (LMS) disease or MI within 24 h of the index procedure (11). More recently, several registries have compared two- (6,12-14) or three-year (15) outcomes in patients undergoing BMS-only versus DES-only PCI, and confirmed higher rates of subsequent revascularization in BMS-treated patients with either lower (12-14) or equivalent (6) rates of mortality or MI in DES-treated patients, or a

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temporal trend in increased mortality with DES (15). In addition, predictors of clinical outcomes in both BMS- (16) and DES-treated (17) patients have been identified; although, for the large part, these studies were again limited to reporting restenosis at six months in patients enrolled in RCTs. With recent concerns raised regarding very late outcomes in patients enrolled in clinical trials, particularly in the context of DES use (18), it is important to examine the long-term outcomes of 'all-comers' who undergo PCI.

In the present study, we sought to examine the long-term clinical outcomes of all patients undergoing PCI at a large, high-volume tertiary care centre. The objective was to determine, through the use of our prospective PCI registry database, the clinical, angiographic and procedural characteristics associated with late mortality and morbidity outcomes of unselected patients in a contemporary PCI practice.

METHODS

The University Health Network PCI registry

Clinical, angiographic, procedural and outcome variables of all patients undergoing PCI at the Peter Munk Cardiac Centre (Toronto, Ontario) are collected prospectively and entered into a data registry by dedicated, specially trained nursing personnel, as described previously (19). The main categories of data collected are as follows:

1. Patient characteristics (age, sex, height, weight, smoking history, hypertension, hypercholesterolemia, diabetes mellitus, previous MI, previous revascularization, baseline creatinine clearance, PCI indication and left ventricular [LV] grade – defined as LV ejection fraction of 60% or greater [grade 1], 40% to 59% [grade 2], 20% to 39% [grade 3], and less than 20% [grade 4]);
2. Procedural variables (number of intervened vessels, American College of Cardiology/American Heart Association [ACC/AHA] lesion type, number of delivered stents, number of undelivered stents, stent diameter and length [millimetres], visual assessment of pre- and post-PCI severity of coronary stenosis, Thrombolysis in Myocardial Infarction flow grade, and use of glycoprotein IIb/IIIa inhibitors [GPII]); and
3. In-hospital outcome variables (cardiac procedural success, abrupt vessel closure, mortality, MI using biomarkers, need for urgent CABG surgery, intra-aortic balloon pump use and arrhythmia; vascular access complications; neurological events; bleeding complications; renal function; and duration of hospital stay after the procedure).

All patients undergoing their first PCI procedure at the University Health Network between April 2000 and September 2007, and who had an Ontario health card were included. The study was approved by the institutional research ethics boards of the University Health Network and the Institute for Clinical Evaluative Sciences in Ontario.

Procedures were undertaken according to standard guidelines and operator preference, with operator choice of stent and technique. Heparin was routinely used as an anticoagulant for all patients, and titrated to keep the activated clotting time at 250 s to 350 s. All patients were premedicated with acetylsalicylic acid (81 mg for elective procedures, and 325 mg for ST elevation MI). Clopidogrel was given as indicated by guidelines that were current at the time: loading was 300 mg to 600 mg, and maintenance occurred for six weeks to 12 months depending on stent type and clinical indication.

In-hospital outcomes and definitions

In-hospital mortality and morbidity rates were calculated for the cohort. Complications were defined according to the ACC/AHA cardiac catheterization standards (20). The definition of periprocedural MI was more inclusive than that of the ACC/AHA criteria, including all patients with creatine kinase elevations two or more times the upper limit of normal. Indications for PCI were defined as follows: elective; primary; postlysis including facilitated or rescue PCI (failure to reperfuse or reinfarction after thrombolytic therapy in the setting of ST elevation MI); and urgent acute coronary syndrome

(ACS) PCI (any procedure for non-ST elevation ACS or occurring more than 48 h after ST elevation MI).

Late outcomes

Long-term follow-up data were obtained through linkage of the clinical database to the Discharge Abstract Database of the Canadian Institute for Health Information and the Registered Persons Database using encrypted health card numbers. All time-to-event analyses were conducted at the ICES in Ontario. Data were available on time-to-event for all-cause mortality, repeat PCI or subsequent CABG surgery, as well as hospitalization for MI, heart failure or stroke (defined by primary *International Statistical Classification of Diseases and Related Health Problems, 10th Revision* hospital coding for admission). Late outcomes were defined as all-cause mortality (including procedural and in-hospital deaths), revascularization (repeat PCI or CABG surgery), late major adverse cardiac events (MACEs) (death or revascularization) and cardiovascular events (CVEs) (death, revascularization, acute MI, heart failure and stroke).

Whole-group unadjusted survival rates were calculated. Kaplan-Meier analysis was performed for the presence or absence of various clinical or procedural characteristics known or hypothesized to be associated with survival post-PCI: sex, LV function, diabetes, cardiogenic shock (defined as a sustained systolic blood pressure of lower than 90 mmHg requiring mechanical or inotropic support), incomplete revascularization (defined as fewer vessels that were treated than were diseased [more than 70% stenosis in an epicardial vessel assessed angiographically]), LMS intervention, residual stenosis of more than 20% assessed angiographically, and BMS versus DES use.

Statistical analysis

All data analyses were performed using SAS version 8.2 (SAS Institute Inc, USA) statistical software. Descriptive statistics were used for continuous variables including mean, median, SD and standard error. Frequencies were used for categorical variables. Univariate comparisons included unpaired *t* tests and contingency table analyses for categorical variables. Kaplan-Meier analysis was used to calculate cumulative probabilities for time-to-event outcomes. Cox multiple regression analysis was performed to identify independent predictors of late mortality, late revascularization and late CVE by entering all variables that had a univariate association with any outcome at $P < 0.25$ or those of known clinical significance but failing to meet the critical alpha level for submission to the model. Variables entered are listed in Appendix A. The alpha for variable retention in multivariable models was 0.10.

RESULTS

Between April 2000 and September 2007, the clinical, angiographic, procedural and outcome variables of 15,012 consecutive patients undergoing PCI at the Peter Munk Cardiac Centre were entered into a prospective database. The first procedure that each patient underwent was included in the study sample ($n=12,864$). Patients with no Ontario health card (out-of-province patients, $n=182$) were not included in the study. The final study sample had a 98.6% complete follow-up rate to March 31, 2008 ($n=12,662$).

Clinical, procedural and angiographic characteristics

Baseline clinical, angiographic and procedural characteristics are shown in Table 1. The majority were men younger than 75 years of age. The present cohort represented a high-risk group – 28% had diabetes, 25% had evidence of significant pre-existing renal impairment (creatinine clearance of less than 60 mL/min) and 61% had multi-vessel disease. The majority of procedures undertaken were for urgent indications rather than elective cases. Cardiogenic shock was the indication for PCI in 1.3% of patients.

In-hospital outcomes

Procedural and in-hospital outcomes are shown in Tables 2 and 3. The in-hospital mortality rate was 1.2%, with a MACE (defined as death, MI or same-stay CABG surgery) rate of 3.1%. The predominant component

TABLE 1
Baseline clinical, angiographic and procedural characteristics of patients (n=12,662)

Variable	
Age, years, mean $\pm$ SD	63 $\pm$ 12
Age >75 years	2401 (19)
Female sex	3499 (27.6)
Body mass index, kg/m ² , mean $\pm$ SD	28.5 $\pm$ 5.0
Body mass index <25 kg/m ²	3021 (23.8)
CCS class IV	6737 (53.2)
Diabetes	3488 (27.6)
Hypertension	7875 (62.2)
Smoker (any)	7559 (59.7)
Hyperlipidemia	9244 (73.0)
Family history of ischemic heart disease	4317 (34.2)
Peripheral vascular disease	1081 (8.5)
LV grade 4 (<20% ejection fraction)	247 (1.95)
Renal impairment (CrCl <60 mL/min)	3205 (25.3)
Percutaneous coronary intervention indication*	
Elective	5944 (46.9)
Urgent	6718 (53.1)
Primary	306 (2.4)
Postlysis	457 (3.6)
Cardiogenic shock	164 (1.3)
Myocardial infarction within 30 days of index admission	4092 (32.3)
Previous coronary artery bypass grafting surgery	1858 (14.7)
Left main stem interventions	453 (3.6)
Multivessel disease [†]	7724 (61)

Data presented as n (%) unless otherwise indicated. *For percutaneous coronary intervention indication, see text for definitions; [†]Multivessel disease defined as stenosis of greater than 70% present in one or more major epicardial artery. CCS class IV Canadian Cardiovascular Society classification of angina; CrCl Estimated creatinine clearance; LV grade Left ventricular function grade on echocardiography or angiography

of MACE was an in-hospital MI rate of 2.6%. The mean ($\pm$ SD) hospital length of stay following PCI was 1.8 $\pm$ 3.7 days (range zero to 166 days, median 1.0 day).

Late outcomes

Survival: The mean follow-up period was 3.7 $\pm$ 2.2 years (range zero to 7.75 years). Late clinical outcomes are shown in Table 4. All-cause mortality at seven years was 10.6%, with a late MACE (defined as any death or repeat revascularization) rate of 26.1%. The late CVE (death, repeat revascularization, acute MI, heart failure and stroke) rate was 31.4%. The unadjusted survival rate estimated by Kaplan-Meier analysis was 83% for the group over the seven-year follow-up period (Figure 1).

Kaplan-Meier survival curves are shown in Figure 2. Men demonstrated a significant survival advantage compared with women (84 $\pm$ 1% versus 82 $\pm$ 1%, $P<0.001$), and survival was directly proportional to the level of LV dysfunction present at the time of index procedure (LV grade 1 or 2, 86 $\pm$ 1%; grade 3, 71 $\pm$ 2%; and grade 4, 49 $\pm$ 45%, $P<0.001$). The presence of diabetes (75 $\pm$ 1% versus 86 $\pm$ 1%, $P<0.001$) and cardiogenic shock (40 $\pm$ 5% versus 84 $\pm$ 1%, $P<0.001$) were both associated with a higher mortality rate. Procedural factors resulting in better survival included complete revascularization (87 $\pm$ 1% versus 78 $\pm$ 1%, $P<0.001$), residual stenosis of less than 20% (84 $\pm$ 1% versus 78 $\pm$ 2%, $P<0.001$), single-vessel rather than multivessel PCI (84 $\pm$ 1% versus 80 $\pm$ 1%, $P<0.001$) and intervention not involving the LMS (84 $\pm$ 1% versus 60 $\pm$ 5%, $P<0.001$). The use of GPIs (84 $\pm$ 1% versus 79 $\pm$ 2%, $P<0.001$) and deployment of DES rather than BMS (91 $\pm$ 1% versus 89 $\pm$ 1%, $P=0.002$) were both associated with better long-term survival.

By multivariate analysis (Figure 3), the presence of cardiogenic shock (HR=3.22, 95% CI 2.4 to 4.2; $P<0.001$) or severe LV dysfunction

TABLE 2
Procedural and angiographic characteristics

Variable	
No lesions treated, mean $\pm$ SD	1.64 $\pm$ 0.9
No vessels treated, mean $\pm$ SD	1.28 $\pm$ 0.6
1 vessel treated	9843 (77.7)
2 vessels treated	2359 (18.6)
3 vessels treated	223 (1.8)
Vessels treated	
Left main stem	248 (1.96)
Left anterior descending coronary artery	6356 (50.2)
Left circumflex coronary artery	4251 (33.6)
Right coronary artery	4835 (38.2)
Saphenous vein graft	715 (5.6)
Lesion type C	5169 (40.8)
Baseline TIMI <3	2913 (23.0)
Post-TIMI 3	12,195 (96.3)
Intra-aortic balloon pump	95 (0.75)
Stent use	12,106 (95.6)
Drug-eluting stent	2888 (22.9)
Number of stents, mean $\pm$ SD	1.77 $\pm$ 1.0
Glycoprotein IIb/IIIa use during procedure	10,461 (82.6)
Fluoroscopy time, min, mean $\pm$ SD	18.2 $\pm$ 13.7
Contrast used, mL, mean $\pm$ SD	330.7 $\pm$ 178.2
Multivessel percutaneous coronary intervention*	2819 (22.3)
Undelivered stents [†]	504 (4.0)
Incomplete revascularization [‡]	5025 (39.7)

Data presented as n (%) unless otherwise indicated. *Delivery of stents to two or more epicardial arteries; [†]Intention but failure to successfully deploy a stent in a desired location; [‡]Defined as fewer vessels treated than were diseased (greater than 70% stenosis in epicardial vessel). TIMI Thrombolysis in Myocardial Infarction

TABLE 3
In-hospital outcomes

Variable	n (%)
All-cause mortality	153 (1.2)
Any myocardial infarction	331 (2.6)
Same-stay CABG surgery	70 (0.55)
MACE	392 (3.1)
Any complication	1025 (8.1)
Abrupt closure	47 (0.4)
Access site complication	222 (1.8)
New dialysis	9 (0.07)
Neurological complication	35 (0.3)

MACE Major adverse cardiac events (death, repeat revascularization by percutaneous coronary intervention or coronary artery bypass grafting [CABG], or myocardial infarction)

(grade 4) (HR=2.93, 95% CI 2.3 to 3.7, $P<0.001$) were the strongest independent predictors of late mortality, and were both associated with a greater than threefold increased risk of mortality. A history of renal dysfunction, peripheral vascular disease, diabetes, hypertension, increasing age and multivessel disease were also predictive of a poor long-term outcome. Procedural characteristics associated with increased mortality included incomplete revascularization, undelivered stents, residual epicardial stenosis postprocedure of greater than 20% and emergent PCI. The use of DES (HR=0.74, $P<0.001$) and GPI (HR=0.81, $P=0.006$) were associated with a significant risk reduction for mortality.

Freedom from revascularization and CVEs

At seven years, 76% of the population was free from recurrent revascularization by either PCI (81 $\pm$ 5%) or CABG surgery (94 $\pm$ 3%). Residual

TABLE 4
Late clinical outcomes

Variable	n (%)	Rate per 1000 patient years
All-cause mortality	1339 (10.6)	28
Repeat PCI	1792 (14.2)	38
CABG surgery	527 (4.2)	11
Any revascularization	2180 (17.2)	46
AMI admission	917 (7.2)	19
HF admission	537 (4.2)	19
Stroke admission	239 (1.9)	5
MACE	3303 (26.1)	70
CV event	3980 (31.4)	84

AMI admission indicates admission to hospital with an acute ST elevation myocardial infarct; CV event Combined cardiovascular events (death, revascularization, acute myocardial infarction, heart failure or stroke); HF admission indicates admission to hospital with heart failure; MACE Major adverse cardiac event (death, revascularization by percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG]); Stroke admission indicates admission to hospital with a major cerebrovascular event

Figure 1 Kaplan-Meier curve estimating overall survival. Estimated unadjusted survival is shown for the whole cohort. PCI Percutaneous coronary intervention

epicardial stenosis and multivessel disease were significant independent predictors of the need for repeat procedures. Other factors – including a history of previous revascularization, diabetes, incomplete revascularization at index procedure, female sex, urgent PCI and less than Thrombolysis in Myocardial Infarction 3 epicardial flow preprocedure – were weakly predictive of further revascularization. DES use was associated with a significant risk reduction for further PCI or CABG surgery (Figure 4).

Freedom from all CVDs was 59% at seven years (Figure 5). Freedom from hospital admission for acute MI was $91 \pm 3\%$, and $94 \pm 3\%$ for admission due to decompensated heart failure. Cardiogenic shock emerged as the most significant independent predictor of late CVDs, increasing risk more than twofold ($HR=2.18$, 95% CI 1.7 to 2.7; $P<0.001$). DES use was associated with a reduced risk of late CVD ($HR=0.77$, 95% CI 0.71 to 0.85; $P<0.001$) (Figure 6).

DISCUSSION

The primary goal of the present study was to describe the late clinical outcomes of patients undergoing contemporary PCI based on a large, prospective registry. We demonstrated that contemporary PCI in a cohort of unselected patients referred to a single centre was associated with excellent long-term outcomes. Survival at seven years was high, and long-term MACE rates were low and consistent with outcomes from RCTs, reflecting the safety of PCI in this high-risk population.

Figure 2 A Kaplan-Meier curves estimating survival. Estimated unadjusted survival is shown for the whole cohort stratified by sex, left ventricular function (where left ventricular ejection fraction of 60% or greater [left ventricular grade (LVG) 1], 40% to 59% [LVG 2], 20% to 39% [LVG 3] and less than 20% [LVG 4]), the presence or absence of diabetes (DM), and the presence or absence of cardiogenic shock. B Kaplan-Meier curves estimating survival. Estimated unadjusted survival is shown for the whole cohort stratified by complete versus incomplete revascularization (defined as residual significant disease – greater than 70% stenosis in epicardial vessel, assessed angiographically – at the end of the procedure), left main (LM) stem stenting versus no LM stem stenting, the presence or absence of residual stenosis (RS) of greater than 20% in any treated vessel immediately postprocedure, and the use of bare-metal stenting (BMS) versus a drug-eluting stent (DES)

In contrast to randomized trials, the present study described very late clinical outcomes and their predictors in a large cohort of 'all-comers'. At seven years, all-cause mortality was 10.6% and repeat revascularization (PCI or CABG surgery) was 17.2%. Our results are comparable with registry data of approximately 1500 unselected patients receiving sirolimus-eluting stents (9) and a pooled analysis from a four-year follow-up of patients enrolled in the Sirolimus-coated Bx Velocity balloon-expandable stent in the treatment of patients with de novo coronary artery lesions (SIRIUS) trials (21). Total cumulative CVDs including admission for acute MI, heart failure or stroke, in addition to repeat revascularization, were high (31.4%) but reflected the relative complexity of the cohort.

The proportion of diabetic patients, patients older than 75 years of age, and those with renal impairment, multivessel disease and LMS involvement, as well as the large burden of high-risk procedural characteristics (multivessel PCI, residual stenosis and incomplete revascularization) found in the study population highlight the complex nature of

Figure 3) Multivariate predictors of late mortality. Cox multiple regression analysis was used to determine independent predictors of late all-cause mortality by entering all variables that had a univariate association with any outcome at $P < 0.25$ or those of known clinical significance but failing to meet the critical alpha level for submission to the model. Variables entered are listed in Appendix A. The alpha for variable retention in multivariable models was 0.10. HRs and P values are displayed for each variable. BMI Body mass index; GPI Glycoprotein IIb/IIIa inhibitor; LV Left ventricular; NYHA New York Heart Association class; PCI Percutaneous coronary intervention; PVD Peripheral vascular disease

disease presenting in everyday practice. Additionally, more than one-half of the procedures (53%) were performed urgently, with 1.3% of patients presenting in cardiogenic shock. The present patient population is not generally well represented in RCTs, although evidence for the role of PCI, particularly with DES, in specific high-risk subsets can be inferred from various subgroup analyses (22) and smaller targeted trials (23,24).

Our data suggest that late unadjusted cumulative survival was significantly worse in women and diabetic individuals, and was directly proportional to the degree of LV dysfunction. This observation is consistent with one-year data reported previously (9,10) from DES registries. Consistent with other studies (9,10,13), the presence of diabetes was associated with higher rates of revascularization procedures. When late CVEs were assessed, the presence of cardiogenic shock and severe LV dysfunction were again most significantly predictive of adverse events, with clinical markers of extensive disease such as diabetes, peripheral vascular disease and LMS involvement also independently associated with a higher event rate. This may suggest that late outcome in these patients is related as much to the state of underlying atherosclerosis as to the procedural success of a particular intervention.

In the present analysis, we found that a suboptimal procedural result with incomplete revascularization or residual stenosis of greater than 20% was associated with significantly worse long-term survival. Although pre-existing clinical factors (cardiogenic shock, severe LV dysfunction, peripheral vascular disease, diabetes, renal dysfunction, increasing age and requirement for emergent PCI) independently predicted late mortality, such procedural characteristics

Figure 4) Multivariate predictors of revascularization by percutaneous coronary intervention or coronary artery bypass grafting. Cox multiple regression analysis was used to determine independent predictors of late revascularization by entering all variables that had a univariate association with any outcome at $P < 0.25$ or those of known clinical significance but failing to meet the critical alpha level for submission to the model. Variables entered are listed in Appendix A. The alpha for variable retention in multivariable models was 0.10. HRs and P values are displayed for each variable. GPI Glycoprotein IIb/IIIa inhibitor; LV Left ventricular; MI Myocardial infarction; TIMI Thrombolysis in Myocardial Infarction

were also independently predictive of long-term outcomes. Some of these procedural characteristics (multivessel PCI, undelivered stents and residual stenosis) may reflect the burden of coronary disease in these patients, rather than merely problems with technical aspects of the procedure. In addition, the strongest independent predictors of the need for late revascularization were procedural rather than clinical in nature. Residual stenosis of greater than 20% in the treated artery was most significantly associated with repeat PCI or CABG surgery, although multivessel PCI and a history of PCI (due to atherosclerotic burden and/or restenosis) were also strongly predictive of the need for further procedures.

Coronary stenting occurred in 96% of all procedures, and DES were deployed in 23% of cases. When comparing patients from mid-2003 onward – the time at which DES became available at our institution – unadjusted cumulative survival at four years was $91 \pm 1\%$ in DES-treated patients versus $89 \pm 1\%$ in patients who received BMS. The results of our study suggest that the use of DES was associated with significantly improved late outcomes, demonstrating increased survival, decreased CVEs and reduced repeat revascularization events. While the superiority of DES in reducing target vessel revascularization is well established, the observation that DES are associated with improved survival has not been substantiated in randomized trials that eliminate selection bias. However, recently published registries have reported similar data in Ontario (12) and Massachusetts (13) – populations with very different health care systems and practices. Tu et al (12) demonstrated an absolute all-cause mortality reduction at three years between patients treated with BMS (7.8%) and those who received DES (5.5%), while Mauri et

Figure 5 Kaplan-Meier curve estimating overall freedom from cardiovascular (CV) events. Estimated long-term freedom from CV events is shown for the whole cohort. Late CV events is a composite end point defined as death, revascularization or hospital admission for acute myocardial infarction, heart failure or stroke. PCI Percutaneous coronary intervention

al (13) reported a mortality benefit at two years. Evidently, any absolute mortality benefit attributable to DES would need to be confirmed by a randomized study with long-term follow-up. It is hypothesized that this mortality benefit may, in part, be explained by a reduction in the need for repeat procedures (with a small subsequent reduction in procedure-related mortality), and a possible benefit associated with prolonged dual antiplatelet therapy in patients receiving DES (13).

Another finding of significant interest was that the use of GPIs during PCI was associated with reduced late cardiac events. GPIs have been demonstrated to improve early outcomes in both elective (25) and high-risk (26,27) PCI patients, and there is evidence for their efficacy up to three years (28). This therapy is used more often at our institution in higher risk patients, and in those undergoing urgent or emergent procedures. Therefore, although a selection bias exists in the use of GPIs, it might be expected to be associated with worse clinical outcomes. The mechanism by which transient and early use of a GPI leads to reduced long-term MACE is unclear, but may relate to long-term vessel healing and stability as well as reducing the early post-PCI events associated with reduced long-term mortality (27).

Limitations

The present study has several important limitations. It describes a single-centre experience and lacks the obvious advantages of a multicentre, multinational randomized study. It is unlikely, however, that a randomized study will be conducted in the context in which the present study was performed, with virtually no exclusion criteria. Despite reporting outcomes from a large prospective registry, our study also suffers from the limitations of retrospective, observational data. Specifically, we cannot account for all possible confounding factors and, because follow-up data were collected from linkage to a provincial administrative database, we cannot report on certain types of data – such as causes of death, types of clinical presentation for subsequent revascularization (ACS, non-ST elevation myocardial infarction, elective, etc) – or specify target-vessel revascularization. In addition, the cohort did not include a high number of primary PCI procedures because this procedure was not introduced as the standard of care in our centre until 2008. All procedures, including stent and pharmacotherapy choice, were at the discretion of the operator and, therefore, open to bias. As a result, the present Toronto-based registry may not be widely applicable to other health care systems or regions where treatment decisions differ.

CONCLUSIONS

The present study reported the late clinical outcomes of all patients undergoing contemporary PCI in a high-volume tertiary care centre.

Figure 6 Multivariate predictors of late cardiovascular events. Cox multiple regression analysis was used to determine independent predictors of late cardiovascular events by entering all variables that had a univariate association with any outcome at $P<0.25$ or those of known clinical significance but failing to meet the critical alpha level for submission to the model. Variables entered are listed in Appendix A. The alpha for variable retention in multivariable models was 0.10. HRs and P values are displayed for each variable. LV Left ventricular; NYHA New York Heart Association class; PVD Peripheral vascular disease

Several procedure-related variables, such as incomplete revascularization and residual stenosis of greater than 20%, as well as established clinical characteristics such as diabetes, multivessel disease and LV dysfunction, are associated with worse late outcomes following PCI. Furthermore, the use of DES and GPI are both associated with late mortality benefit. These findings, which are reflective of real-world practice, may help clinicians further characterize and better treat high-risk patients who are undergoing PCI.

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APPENDIX A

Variables entered into the multivariate analysis model

Age by decade ≥ 50 years
Female sex
Urgent priority
Primary percutaneous coronary intervention (PCI)
Cardiogenic shock (defined as a sustained systolic blood pressure of lower than 90 mmHg requiring mechanical or inotropic support)
Failed thrombolysis (failure at 90 min of ST segment elevation to resolve by $>50\%$, necessitating 'rescue PCI')
Left ventricular grade 3 (ejection fraction 20% to 40%)
Left ventricular grade 4 (ejection fraction $<20\%$)
New York Heart Association class IV
Myocardial infarction <30 days before PCI
Renal dysfunction (creatinine clearance <60 mL/min)
Diabetes
Hypertension
Hyperlipidemia
Peripheral vascular disease
Thrombocytopenia
Previous revascularization (coronary artery bypass grafting or PCI)
Body mass index <25 kg/m²
Type C lesion
Thrombolysis in Myocardial Infarction (TIMI) flow <3
Drug-eluting stent
Glycoprotein IIb/IIIa inhibitor
Multivessel PCI
Left main PCI
Incomplete revascularization (defined as fewer vessels treated than were diseased ($>70\%$ stenosis in a major epicardial vessel assessed angiographically))
Residual stenosis $>20\%$

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