Incidence and Predictors of Contrast Induced Nephropathy after Percutaneous Coronary Intervention for Chronic Total Occlusion

Thesis

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List of Contents

List of Tables

Table No.	Title	Page No.

List of Figures

List of Abbreviations

Abb.	Full term
ACC	: American College of Cardiology
AHA	: American Heart Association
AUC	: Area under the curve
CABG	: Coronary artery bypass grafting
CHF	: Congestive heart failure
CIN	: Contrast induced nephropathy
CKD	: Chronic kidney disease
CM	: Contrast media
CTO	: Chronic total occlusion
CTOs	: Coronary chronic total occlusions
EACTS	: European Association for Cardio Thoracic Surgery
eGFR	: Estimated glomerular filtration rate
ESC	: European Society of Cardiology
ESUR	: European Society of Urogenital Radiology
GFR	: Glomerular filtration rate
HOCM	: High osmolar contrast media
HS	: Highly significant
IOCM	: Iso-osmolar contrast media
LDL-c	: Low density lipoprotein–cholesterol
LOCM	: Low osmolar contrast media
LV	: Left ventricular
MDRD	: Modification of Diet in Renal Disease
MI	: Myocardial infarction
NAC	: N-Acetylcysteine
NS	: Non significant
NSAIDs	: Non-steroidal anti-inflammatory drugs
NYHA	: New York Heart Association classification
PCI	: Percutaneous coronary intervention
ROC	: Receiver operating characteristic curve
S	: Significant
SCr	: Serum creatinine
SPSS	: Statistical package for Social Science
TIMI	: Thrombolysis in myocardial infarction

INTRODUCTION

There have been numerous technical and pharmacological advances in the field of percutaneous coronary intervention (PCI) since its introduction many years ago ***(Stone et al., 2005).***

PCI for chronic total occlusions (CTO) remains a challenge for the interventional cardiologist because of lower procedural success rates compared to PCI for non-occlusive lesions ***(Di Mario et al., 2007).***

CTO is defined according to thrombolysis in myocardial infarction (TIMI) score as (grade0-1) flow with a duration>3 months, documented angiographically ***(Barlis et al., 2008).***

Iodinated contrast media are being used increasingly in the catheterization laboratory during diagnostic catheterization and PCI, Contrast induced nephropathy (CIN) is a major cause of morbidity and mortality associated with PCI ***(Rihal et al., 2002).***

CIN was defined as increase in the baseline creatinine levels ≥0.5 mg/dl (≥44.2 μmol/l) or ≥25% in the 48 hr following the procedure ***(Dangas et al., 2005).***

Known predictors of CIN include age, anemia, diabetes mellitus, severe heart failure or hypotension, previous chronic

renal failure and large volumes of contrast ***(Mehran et al., 2004).***

Certain procedural variables can also increase the risk of CIN in patients undergoing coronary angiography with or without PCI these include use of an intra-aortic balloon pump, contrast media dose and the type of contrast medium used ***(Aspelin et al., 2003).***

AIM OF THE WORK

To assess the incidence and predictors of contrast induced nephropathy (CIN) after percutaneous coronary intervention (PCI) for chronic total occlusion (CTO).

I - CONTRAST INDUCED NEPHROPATHY

Radiologic procedures utilizing intravascular iodinated contrast media (CM) injections are being widely applied for both diagnostic and therapeutic purposes ***(Gruberg et al., 2000)***.

This results in the rising incidence of iatrogenic renal function impairment caused by the exposure to CM, a condition known as contrast induced nephropathy (CIN) **(*Nash et al., 2002*)**.

This iatrogenic complication has been a subject of concern to cardiologists in recent years because of its adverse effect on prognosis and addition to health care costs. At the same time, many hospitalized patients have compromised renal function ***(Chew et al., 2006)***.

⊙ Definition:

CIN is implied when there is a temporal link between deterioration of renal function and the administration of I.V. contrast, in the absence of any other etiology ***(Barrett et al., 2006).***

While there is no universally accepted definition of CIN, it is usually recognized by an acute deterioration in renal function 2 to 7 days following contrast administration, which

occurs in the absence of other identifiable causes of acute renal failure ***(Gleeson et al., 2004)***.

CIN is typically defined in the recent literature as an increase in serum creatinine (SCr) occurring within the first 24 h after contrast exposure and peaking up to 5 days afterwards. In most instances, the rise in SCr is expressed either in absolute terms (0.5 to 1.0 mg/dl) or as a proportional rise in SCr of 25% or 50% above the baseline value **(*McCullough et al., 2008)***.

The most commonly used definition in clinical trials is a rise in SCr of 0.5 mg/dl or a 25% increase from the baseline value, assessed at 48 h after the procedure **(*McCullough et al., 2008)***.

The European Society of Urogenital Radiology (ESUR) defines CIN as impairment in renal function (an increase in serum creatinine by more than 25% or 44.2 μmol/l [0.5 mg/dl]) within 3 days after intravascular administration of contrast medium, without an alternative etiology **(*Thomsen et al., 2003)***.

The Acute Kidney Injury Network definition is a rise in SCr >0.3 mg/dl with oliguria, which is compatible with previous definitions **(*Thomsen et al., 2003)***.

Typically, CIN onset occurs within 24–48 hours of exposure, SCr levels peak in 3–5 days, and renal function returns to baseline in 7–21 days ***(Solomon et al., 1998*)**.

If renal function does not return to baseline, other possible causes of renal injury like atheroembolism should be suspected **(*Solomon et al., 1998)***.

It is important to note that these are relatively nonspecific definitions, and there are no biomarkers that differentiate CIN from other potential causes of acute renal failure, such as atheroembolic disease arising from vascular manipulation ***(Gleeson et al., 2004)***.

⊙ Epidemiology:

Radiographic CM are responsible for 11% of cases of hospital-acquired renal insufficiency, the third most common cause of renal failure after impaired renal perfusion and the use of nephrotoxic medications ***(Nash et al., 2002)***.

Among all procedures utilizing CM for diagnostic or therapeutic purposes, coronary angiography and percutaneous coronary interventions (PCI) are associated with the highest rates of CIN ***(Nash et al., 2002)***.

The overall incidence of CIN after PCI has been reported between 3.3% and 16.5%, although this figure increases up to 50% in high-risk patients **(*Recio-Mayoral et al., 2007)***.

Patients encountered in interventional cardiology practice have multiple risk factors for CIN, such as renal impairment (with and without diabetes), congestive heart failure, reduced arterial pressure, and concurrent use of nephrotoxic medications, and in such patients the incidence of CIN has been reported to range between 11% and 50% **(*Rihal et al., 2002)***.

In the interventional cardiology registry from Mayo Clinic including 7586 patients, the incidence of CIN was 3.3% **(*Rihal et al., 2002)***.

In a smaller study from William Beaumont Hospital, among 1826 patients treated with PCI, CIN occurred in 14.5% of the cases ***(McCullough et al., 1997).***

Fortunately, among patients undergoing PCI, cases of CIN leading to dialysis are rare (0.5 to 2 percent). However, when they occur, they are related to catastrophic outcomes including a 36 percent in-hospital mortality rate and a 2-year survival of only 19 percent **(*Pannu et al., 2006)***.

The frequency of CIN has decreased over the past decade; this is due to a greater awareness of the problem, better

risk prevention measures, and improved iodinated contrast media with less renal toxicity. However, many cases of CIN continue to occur because of the ever-increasing numbers of procedures requiring contrast **(*McCullough et al., 2008)***.

In patients undergoing primary PCI for myocardial infarction (MI), short- and long-term mortality rates were also significantly higher in those who developed CIN ,Furthermore, in this group, it has been shown that CIN is an independent predictor of mortality **(*Marenzi et al., 2004)***.

⊙ Pathogenesis:

The exact underlying mechanisms of CIN are likely to involve the interplay of several pathogenic factors (Figure 1). Intrinsic causes include the following: increased vasoconstrictive forces, decreased local prostaglandins and nitric oxide mediated vasodilatation, a direct toxic effect on renal tubular cells with damage caused by oxygen free radicals, increased oxygen consumption, and increased intra-tubular pressure secondary to contrast induced diuresis, increased urinary viscosity and tubular obstruction, all culminating in renal medulla ischemia. Intrinsic causes act in concert with harmful extrinsic (pre-renal) causes such as dehydration and decreased effective intravascular volume ***(Bakris et al., 1990)*.**