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Predictors of Contrast induced Nephropathy Following Percutaneous Coronary Intervention in Patients with Chronic Total Occlusion

Thesis

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Talal A. Elshafei

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List of Abbreviations

Abb.	Full term
AHF	Acute heart failure
AKI	Contrast induced acute kidney injury
AUC	Area under the ROC curve
CIN	Contrast induced nephropathy
CKD	Chronic kidney disease
CM	Contrast media
CTO	Chronic total occlusion
DM	Diabetes mellitus
EF	Ejection Fraction
GFR	Glomerular filtration rate
Hx	History
MI	Myocardial infarction
NO	Nitric oxide
PCI	Percutaneous coronary intervention
RAAS	Renin angiotensin aldosterone system
ROC	Receiver-operating characteristic
SB	Side branch
SPSS	Statistical package for social sciences
TIMI	Thrombolysis in Myocardial Infarction

INTRODUCTION

Contrast induced nephropathy (CIN) is one of the agreed upon complications of procedures that foresee the use of contrast media, recognized as a leading cause of morbidity and mortality in patients undergoing percutaneous coronary intervention (PCI) and is commonly defined as an increase in serum creatinine levels; usually ≥ 0.5 mg/dl or ≥ 25% of baseline levels, within 24–48h after contrast exposure ***(Barbieri et al., 2015; Aram et al., 2022).***

The development of CIN after coronary angiography is associated with a long-term poor clinical outcome. CIN has shown to occur in up to 20–25% depending on the presence of known risk factors in patients undergoing diagnostic and/or coronary intervention angiography ***(Barbieri et al., 2015).*** Theoretically speaking chronic total occlusion as part of complex per-cutaneous coronary interventions maybe associated with higher percentage of contrast induced nephropathy. In summarizing previous published data it is agreed that the recognized risk factors for the development of CIN can be divided into two groups: patients' related risk factors or underlining chronic diseases (hypertension, chronic renal failure, diabetes, older age, heart failure, hyperuricaemia, anemia, dehydration, hypoproteinaemia, previous kidney transplant and the use of nephrotoxic drugs such as diuretics or aminoglycosides) and procedural related risk factors (contrast volume, contrast media characteristics, procedure time, vascular

access, two or more consecutive procedures within 72h and the use of intra-aortic balloon pump). Several additional studies have been conducted to identify new risk factors associated with this complication.

However, few data are available at the moment about the relationship between different parameters such as age, gender, vascular access, time of operation, contrast volume, and patients with history of diabetes, hypertension, smoking, bleeding event prior to PCI or patients with HFmrEF as risk factors and the development of CIN in chronic total occlusion (CTO) after PCI procedure ***(Lucreziotti et al., 2014; Silver et al., 2015; Heyman et al., 2013).*** From the theoretical point of view the vascular access in CTO following a different path to coronary arteries, could be associated with different incidence of CIN this is contributed to the fact that transradial approach is associated with longer procedure time and larger amount of contrast material used ***(Alaswad et al., 2015).*** It is also suggested theoretically that the more is the time of operation, the more is the development of CIN.

Aim of the Work

Is to predict the development of contrast induced nephropathy in patients with chronic total occlusion after per-cutaneous coronary intervention.

CHRONIC TOTAL OCCLUSION

Coronary chronic total occlusion (CTO) represents the latest form of coronary artery disease and is gaining an increased attention in medical field. Despite its complex nature, the success rate of CTO procedures and revascularization is improving as a consequence of the introduction of tailored devices and increasing clinical experience of operators ***(Goliasch et al., 2019).***

Definition of Chronic Total Occlusion (CTO).

Chronic total occluded (CTO) was defined as coronary lesions with TIMI (Thrombolysis in Myocardial Infarction) flow grade 0 of at least 3 months' duration ***(Barlis et al., 2008).*** Estimation of the duration of occlusion was clinical, based on the first onset of angina, history of myocardial infarction (MI) in the target vessel territory, or comparison with a prior angiogram.

Success of the CTO procedure was defined as successful CTO revascularization with achievement of <30% residual diameter stenosis within the treated segment and restoration of TIMI antegrade flow grade 3 ***(Tajti et al., 2018).***

Pathophysiology of CTO

In essence, the majority of CTOs result from soft plaque rupture followed by coronary thrombotic occlusion and its subsequent organization. A small amount of CTO lesions results from development of atheroma. Once coronary artery occlusion

happens, frequently the thrombus is propagated in a retrograde pattern from the point of occlusion extending proximally reaching the proximal segment with a major side branch (SB) ***(Srivastsa et al., 1997; Godino et al., 2010).***

This thrombus gets becomes more rigid than fresh thrombus formation, with a dense concentration of collagen-rich fibrous tissue at the proximal and distal ends of the lesions, referred to as proximal and distal fibrous caps, ***(Godino et al., 2010),*** respectively with intervening occluded segments (Table 1). The occluded segment remains biologically active with recanalization, neovascularization, and inflammation giving rise to different forms of CTOs (Table 2) ***(Mishra et al., 2017).***

The earlier CTO lesions are noticed to be predominantly soft or lipid laden whereas older lesions are usually hard or calcific. Short duration CTO showed organized or organizing thrombus and presence of necrotic core. High number of intimal plaque capillaries are observed with increasing occlusion age ***(Srivastsa et al., 1997).***

Table 1: Chronological pathology of a coronary chronic total occlusion

1. Acute phase: Obstructed lumen typically consists of ruptured plaque and thrombus.
2. Early phase: Deposition of proteoglycan matrix
3. Late phase: Negative remodeling consisting of dense collagen and calcium deposit
4. Late phase: Without negative remodeling, the presence of large micro-channels suitable for wire crossing

In CTOs less than one year old, the adventitia is the predominant vessel wall location of neovascular channel formation in terms of both size and number. In CTOs more than one year old, intimal plaque capillary numbers and size increase and are not significantly different from adventitia. The high frequency of large neovascular channels in all vessel wall locations even in CTOs of less than one year old duration reflects that the enlargement of growing neovascular channels within CTO is an early event ***(Dash et al., 2018).***

The success of guidewire crossing in CTO PCI might be affected by

- Loose fibrous tissue
- Pultaceous debris
- Intimal plaque microchannels

Table 2: Histological components of chronic total occlusion

Consistency	Components of occlusion
Very soft	Recanalized lumen, microchannels
Soft	Thrombus, proteoglycans, cholesterol clefts
Firm	Collagen, elastin
Hard	Calcium

CTOs exhibit two types of histological vascular channels that span the occluded segment ***(Katsuragawa et al., 1993).***

- Endothelialized microchannels (160–230 mm) generated via neovascularization that connects the CTO from proximal to distal cap are termed histologically recanalized segments.

- Micro capillaries (< 100 um) that pass into the small SB or into the vasa vasorum, are termed non-recanalized segments as they do not span the CTO from proximal to distal caps.

Short segment CTO with tapered tip stump is less likely to have a side branch (SB) and more likely to have histologically recanalized segments than longer occlusions. The tissue composition of tapered stump is characteristically looser fibrous tissue, with prominent neovascularization and recanalization. These recanalized segments results in facilitating guidewire entry into distal true lumen within endothelialized microchannels. All occlusions with non-tapered or blunt stump have non-recanalized microcapillaries. Older CTOs have greater calcification and fibrosis, fewer foam cells and macrophages as compared to younger ones showing difficult cannulation (Fig. 1) ***(Dash et al., 2018).***

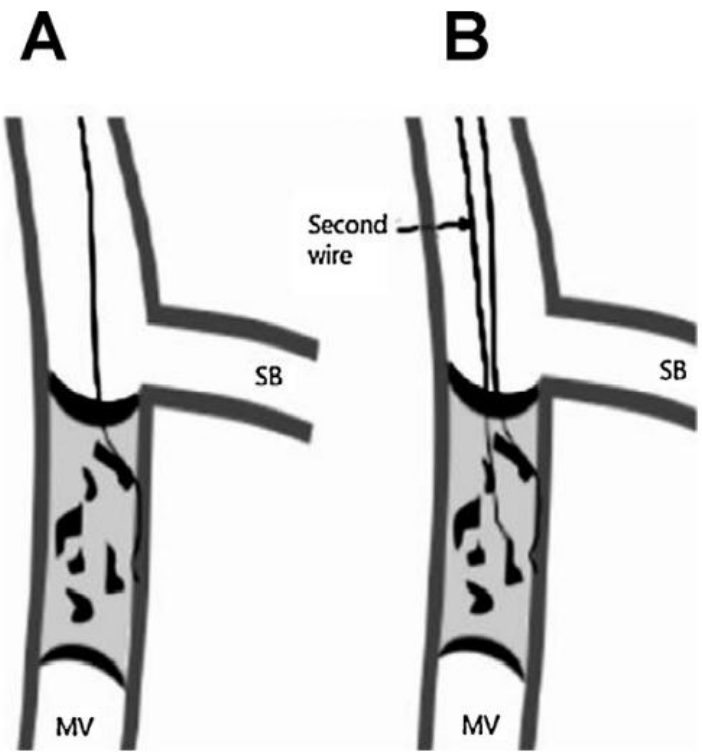

Fig. 1: Long segment CTO with heavy calcium. A) Deflection of guidewire into subintimal space because of heavy calcium. B) Employment of parallel wire (2nd wire being stiffer and tapered tip) technique for successful navigation into true lumen. ***(Dash et al., 2018).***

The CTO has been frequently divided into intimal and subintimal spaces which are the main aspects of pathological information. The subintimal space lies external to the intimal layer but within the vessel structure that includes the media (smooth muscle) and adventitia.

During PCI, subintimal wire passage is within media between internal and external elastic membrane following the path of least resistance. Because of presence of histologically weak connective tissue, dissection in this area spreads widely and