Cardiovascular disease: revascularisation

Date written: May 2013
Author: Helen Pilmore

GUIDELINES

Chronic kidney disease not requiring dialysis

a. We recommend that in patients with chronic kidney disease (CKD), end stage renal failure (ESRF) and after kidney transplantation, that guidelines for revascularisation of the general population be adhered to (1D).

UNGRADED SUGGESTIONS FOR CLINICAL CARE

- Patients with evidence of coronary artery disease should be referred to a cardiologist for expert opinion (ungraded)

- Physicians should be aware that revascularisation of coronary arteries with coronary artery bypass graft (CABG) and percutaneous intervention (PCI) is associated with greater mortality and morbidity in patients with chronic kidney disease (CKD) and those on dialysis compared with the general population (ungraded).

IMPLEMENTATION AND AUDIT

Registries of all dialysis patients and patients with CKD undergoing coronary artery revascularization will assist with enlightening the nephrology and cardiology sectors about outcomes after revascularisation.

BACKGROUND

Cardiovascular disease is the leading cause of death in patients with end stage renal failure. The risk of cardiovascular death is significantly reduced in the renal transplant population compared with those on dialysis, but is still significantly greater than that of the general population [1]. In addition, the risk of cardiac death and major cardiac events is greater in those with CKD than those with normal renal function [2, 3].

Revascularisation of coronary artery stenoses has been extensively studied in the general population and guidelines for the management of both unstable [4] and stable [5] coronary artery disease (CAD) have been generated using evidence from randomised controlled trials. However in most trials, patients with significant renal impairment have been excluded.

The data regarding revascularisation of patients with kidney disease is sparse, especially in regards to randomised controlled trials. In contrast there is a large body of data and hence many guidelines in the general population. Both the current ACCF/AHA and European guidelines include special mention of patients with chronic kidney disease.

The aim of this guideline is to review the literature and assess the benefits and harms of revascularisation of CAD in patients with CKD, including the dialysis and transplant populations. The revascularisation literature was examined both in unstable and stable CAD.

SEARCH STRATEGY
Databases searched: MeSH terms and text words for chronic kidney disease, end-stage kidney disease and renal replacement therapy were combined with MeSH terms and text words for cardiovascular disease and then combined with MeSH terms and text words for revascularisation and then combined with the Cochrane highly sensitive search strategy for randomised controlled trials. The search was carried out in Medline. The Cochrane Renal Group Trials Register was also searched for trials not indexed in Medline.

Date of search/es: 19 September 2007 and updated search 23 February 2011 and April 2013.

WHAT IS THE EVIDENCE?

Randomised controlled trials (RCT): There are few RCT examining outcomes after revascularisation in patients with kidney disease. Much of the RCT data is taken from post-hoc analyses of RCT from the general population where patients with CKD were identified and analysed. There are however a large number of guidelines in the general population. Guidelines for the general population examined in this publication are as follows:

- 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients with Stable Ischemic Heart Disease [4]
- European Society of Cardiology (ESC) Guidelines on myocardial revascularization 2010 [7]
- European Society of Cardiology (ESC) Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation 2012 [8]

Revascularisation compared with medical therapy: stable or asymptomatic CAD

General population

There are a number of studies in the general population comparing revascularisation with medical therapy. As a result of these papers, there are clear guidelines for the general population outlining which patients should be revascularised both for survival and symptomatic benefit [4, 7] [ACCF/AHA; ESC]

CKD population

There is only one RCT comparing revascularisation with medical treatment in patients with CKD [9]. All patients had insulin dependent diabetes mellitus (mainly Type I) and underwent coronary angiography as part of the assessment for transplantation listing. Twenty-six patients were randomised to medical treatment (Calcium Channel Blocker (CCB) + aspirin) or revascularisation. The study was powered to enrol 162 patients to detect a 10% improvement with revascularisation. Ten patients in the medically treated group and 2 in the revascularisation group reached cardiac endpoints (unstable angina, myocardial infarct (MI), cardiac death) in a median time of 8.4 months. Three medically treated patients died of MI compared with no deaths from MI in the revascularisation group.

The study was terminated 30 months after recruitment commenced because of both slow patient recruitment and excess events in the medically treated group after an interim analysis at 24 months. The paper does not comment on the severity of CKD nor on the proportion of patients already on dialysis, however, presumably patients had severe CKD as transplantation was being considered. Ten patients (5 in each group) had dialysis initiated during the course of the study.

This study was hampered by low recruitment, low use of beta blockers, the use of short acting CCB and variable aspirin use. In addition, the follow-up was short. The authors conclude that a larger study is needed.
There are no other studies in the renal population, however, a large RCT was performed in patients scheduled for vascular surgery. This group of patients is at very high risk for cardiac events [10]. A total of 510 patients were randomised to pre-operative coronary artery revascularisation (coronary artery bypass graft [CABG] or percutaneous coronary intervention [PCI]) or conservative medical therapy. Patients randomised to revascularisation underwent CABG or PCI prior to their vascular surgery. There was no survival benefit in revascularisation compared with no revascularisation for any subgroup of patients with 6 years of follow-up. Incidentally, there was no difference in the use of statins, beta-blockers, aspirin or angiotensin converting enzyme inhibitors (ACEi) between the two groups.

The COURAGE study [11] enrolled 2287 patients with stable ischemic heart disease in a randomised trial comparing optimal medical treatment (OMT) alone or OMT with percutaneous coronary intervention (PCI). This study found no benefit in PCI over OMT alone. A post hoc analysis of this study examining 320 patients with an eGFR < 60ml/min [b] demonstrated that CKD is an independent predictor of death and non-fatal myocardial infarction. However as for the general population, PCI did not reduce the risk of death or myocardial infarction when used with optimal medical therapy [12].

**Revascularisation compared with medical therapy: unstable CAD**

**General population**

Acute revascularisation of unstable CAD is now considered optimal treatment for patients with acute myocardial infarction in the general population [guidelines].

**CKD population**

A recent meta-analysis examined trials comparing conservative therapy with early intervention in non-ST elevation acute coronary syndromes in patients with CKD [13]. Five trials enrolling 1453 patients were included. Early angiography was not associated with a reduction in all-cause mortality (RR 0.76; 95% CI 0.49 – 1.17; P = 0.21), non-fatal myocardial infarction nor a composite of death and non-fatal MI. There was however a significant reduction in rehospitalisation (RR 0.79; 95% CI 0.66 – 0.87; p< 0.001). Although there was no significant difference in mortality or in non-fatal myocardial infarction, there was a trend to reductions in these endpoints with a comparable magnitude of reduction to that reported in the general population.

**Outcomes of revascularisation**

**Coronary Artery Bypass Grafting (CABG):**

**Chronic kidney disease**

There are a number of studies examining the outcomes of CABG in patients with CKD which is defined using a variety of methods (eGFR, creatinine clearance, serum creatinine). In comparison with the general population, patients with CKD are at increased risk of early [14-17] and late mortality [16, 18-21] after CABG. Estimated GFR is an independent predictor of mortality in patients undergoing CABG (HR 0.80 per 10ml/min per 1.73m2; 95% CI 0.72 – 0.89; P < 0.001) [22]. In addition, the presence of CKD is associated with increased morbidity and complications [23] compared with those with normal renal function. Results from a retrospective study [24] of patients undergoing elective vascular surgery show that patients with end-stage renal disease (ESRD) were significantly more likely to develop surgical site infection (8.0% versus 3.9%; p<0.001), unplanned intubation (4.8% versus 2.0%; p<0.001), ventilator dependence (4.5% versus 2.1%; p<0.001), combined pulmonary outcome (8.6% versus 3.9%; p<0.001), composite outcome (16.5% versus 8.4%; p<0.001), death (7.2% versus 1.4%; p<0.001), and return to the operating room (23.8% versus 8.5%; p<0.001) compared to the non-ESRD group. Patients with ESRD undergoing open abdominal aortic aneurysm repair, carotid endarterectomies and peripheral vascular operations had elevated rates of complications and death compared with the non-ESRD patients.

**Dialysis**

Patients on dialysis have a greater perioperative mortality than those with normal renal function after CABG [25] and markedly reduced long-term survival compared with the general population [26]. Dialysis patients are also more likely to require blood transfusions than those with normal renal function.
There are two large studies of dialysis patients specifically examining revascularisation using registry data [28, 29]. Both studies show poor long term survival from CABG (2 year survival of 56%).

**Transplant**

There are few studies specifically examining CABG in transplant patients. One small study identified a 5-year survival of 85% and less than 10% of patients returning to haemodialysis after CABG [30]. The largest study [31] examining outcomes in 2661 renal transplant recipients found a 2-year survival of 82.7% after CABG with internal mammary artery grafting and a 67% 4-year survival.

**Percutaneous Coronary Intervention**

**Chronic Kidney Disease**

CKD patients treated with PCI using angioplasty are at greater risk of in hospital [32-34], 30 day [35] and long term mortality [32, 33, 36-38] in addition to an increased risk of major cardiac events [38] and cardiac mortality [36] compared with those with normal renal function. Additionally, PCI in patients with CKD appears to be associated with a greater risk of re-stenosis and the requirement for target vessel revascularisation [32, 35, 39].

**Dialysis**

Similarly, patients on dialysis are at greater risk than the general population of 1 and 2-year mortality [36, 39] and appear to be at high risk of re-stenosis [40-42].

**Transplant**

There are no studies specifically comparing the outcomes of transplant recipients after PCI with the general population. Survival at 4 years after PCI was 68.7% in a study including 652 renal transplant recipients [31]. Restenosis has not been examined in the current literature.

**Outcomes of Coronary Artery Stenting**

Drug eluting stents are recommended in the general population due to their beneficial effects of reducing restenosis and requirement for target vessel revascularisation [7]. No reduction in death or myocardial infarction has been proven for drug eluting stents compared to bare metal stents in the general population.

**Chronic Kidney Disease**

There are now a number of studies examining the use of stents in populations of patients with CKD. Lemos examined the use of bare metal (BMS) and drug eluting stents (DES) and compared the outcomes in patients with normal renal function defined as a creatinine clearance of >60mL/min with those with CKD (< 60mL/min). This study [43] found a greater incidence of mortality in the CKD group. In both patients with CKD and normal renal function, there was a reduction in re-stenosis with the use of drug eluting stents compared with bare metal stents. Another larger study [44] compared the use of drug eluting and bare metal stents with the normal and CKD populations. This study showed that CKD was an independent risk factor for target vessel revascularisation. In the overall group, there was an increased incidence of major cardiac adverse events and re-stenosis with the use of bare metal stents. In comparison however, one study [45] examining outcomes with the normal and CKD populations, found no increase in the re-stenosis rate of patients treated with coronary stents compared with the population with normal renal function, although CKD was an independent predictor of both death and myocardial infarction.

More recently Charytan [46] demonstrated a reduction in mortality in a retrospective review of patients with CKD treated with drug eluting stents compared to bare metal stents however after propensity score matching there was no difference in any outcome including target vessel revascularisation. Similar results were found by others [47, 48]. The literature however is conflicted in this area. Tsai [49] undertook a retrospective review of 283,593 patients treated with either bare metal or drug eluting stents. There was increased mortality and myocardial infarction in patients with CKD or dialysis compared to patients with an eGFR of > 60ml/min. There was a reduction in the OR of mortality for patients treated with drug eluting stents for those with an eGFR of >30ml/min but not for patients with worse renal function. The OR for myocardial infarction was reduced with drug eluting stents in all
patients including those on dialysis while there was no difference in the requirement for target vessel revascularisation in patients with any eGFR < 60ml/min.

**Dialysis**

There is little in the literature reporting on the use of stents in dialysis patients and comparing outcomes with a matched group of patients with normal renal function. One study showed an increased incidence of re-stenosis in the dialysis group [43]. Another study, however, [39] reported no difference in the re-stenosis rate between the dialysis and normal renal function populations.

A recent meta-analysis of 869 patients with end stage renal failure in 7 non-randomised trials showed a significant reduction in the risk of target vessel revascularisation with the use of drug eluting stents compared to bare metal stents. Numbers of patients in each study were small and most studies employed the use of sirolimus eluting stents (SES) [50]. More recently Ishii [51] retrospectively examined haemodialysis patients treated with either DES or BMS. There was a reduction in the unadjusted likelihood of all-cause mortality and target vessel revascularisation however no difference was seen for the risk of myocardial infarction or stent thrombosis. Several other studies in dialysis patients have shown lower target lesion revascularisation (TLR) but have been retrospective [52-55]. The Outcome of Cypher stent in Haemodialysis patients (OUCH) study [56] prospectively examined patients with Sirolimus eluting stents demonstrating a 23.9% rate of TLR with some differences in the distribution of lesions. There is one trial randomly assigning dialysis patients to either Sirolimus eluting stents (SES) or Everolimus eluting stents (EES)[57]. This showed a reduction in angiographic restenosis rates in the EES group compared with the SES group although no difference was detected in major adverse cardiac events.

**Transplant**

There is one study examining the use of coronary artery stents using registry data [31]. In this study, 909 transplant recipients underwent CAS. Survival after stenting was 89.4% at 12 months and 72.6% at 4 years. Restenosis using stents has not been specifically examined in the transplant population.

**SUMMARY OF EVIDENCE**

There is limited evidence from RCTs comparing revascularisation with medical therapy specific for patients with CKD. The available data including ad hoc sub group analyses of RCTs conducted in the general population does not currently justify guideline recommendations specific to people with CKD for either stable or unstable CAD.

In comparison with the general population, patients with CKD are at increased risk of early and late mortality after CABG. Patients on dialysis have a greater perioperative mortality than those with normal renal function after CABG and markedly reduced long-term survival compared with the general population.

CKD patients and patients on dialysis treated with PCI using angioplasty are at greater risk of long-term mortality and major cardiac events compared with those with normal renal function.

There are few outcome studies following CABG or PCI that have included transplant recipients and none of these have included control groups for comparison.

There are no RCTs comparing outcomes associated with bare metal stents (BMS) versus drug eluting stents (DES) or different types of DES. Retrospective data for both CKD and dialysis patients is inconclusive in relation to the use of DES compared to BMS and associations with mortality, major cardiac events and restenosis. There are currently insufficient data to support guideline recommendations on the use of DES specific to patients with CKD or those on dialysis. Similarly there has been limited assessment of outcomes following the use of stents in transplant recipients.

**WHAT DO THE OTHER GUIDELINES SAY?**

**INTERNATIONAL GUIDELINES:**
Kidney Disease Outcomes Quality Initiative: No recommendation.
UK Renal Association: No recommendation.
Canadian Society of Nephrology: No recommendation.
European Best Practice Guidelines: No recommendation.
International Guidelines: No recommendation.

SUGGESTIONS FOR FUTURE RESEARCH

Randomised controlled trials comparing different modalities of revascularization (eg CABG compared to Stenting) would assist with guiding decisions regarding the optimum mode of revascularization in patients with CKD.

Finally a RCT comparing conservative treatment with revascularization would assist with decision making regarding treatment of coronary artery disease in patients with CKD.

CONFLICT OF INTEREST

Helen Pilmore has no relevant financial affiliations that would cause a conflict of interest according to the conflict of interest statement set down by CARI.

REFERENCES

### Table 1. Characteristics of included studies

<table>
<thead>
<tr>
<th>Study ID</th>
<th>N</th>
<th>Study design</th>
<th>Description - Participants and Interventions</th>
<th>Follow up (months)</th>
<th>Comments and results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Revascularisation compared with medical therapy: stable or asymptomatic coronary artery disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manske et al 1992 [9]</td>
<td>26</td>
<td>Open label randomised controlled clinical trial</td>
<td>Insulin dependent diabetic candidates for kidney transplantation with coronary artery lesions and suitable for revascularisation. Medical treatment (and aspirin) CCB vs. revascularisation. Primary outcome: unstable angina, MI and cardiac death.</td>
<td>24</td>
<td>CV events in revascularisation group compared to medical treatment: RR: 0.20 (95%CI:0.05, 0.74) \ RD: -0.62 (95%CI:-0.92, -0.31) Limitations: Small single centre trial. Limited to individuals with type 1 diabetes. Terminated early.</td>
</tr>
<tr>
<td>McFalls et al (2004) [10]</td>
<td>510</td>
<td>Open label randomised controlled clinical trial</td>
<td>Patients scheduled for elective vascular operation at an increased risk for perioperative cardiac complications. Coronary artery revascularisation before surgery vs. No coronary artery revascularisation. Primary outcome: long-term mortality.</td>
<td>36</td>
<td>RR in group subject to coronary artery revascularisation compared to no revascularisation before surgery  Death after VA surgery: 0.92 (95%CI: 0.34, 2.50). Control rate: 3.4% Myocardial infarction (total): 0.88 (95%CI:0.62, 1.25). Control rate: 22.8% Stroke: -0.03 (95%CI:-0.10, 0.05). Control rate: 0.8% Limitations: Not a CKD population and there is no measure of renal function to allow sub group assessments.</td>
</tr>
<tr>
<td>Boden et al (2007)[11] [COURAGE Study]</td>
<td>2287</td>
<td>Randomised controlled trial</td>
<td>Patients with myocardial ischemia and coronary artery disease. Percutaneous coronary intervention (PCI) with optimal medical therapy (OMT) versus OMT alone. Primary outcome: death from any cause and non-fatal myocardial infarction</td>
<td>55.2 (median)</td>
<td>There were no significant differences between the PCI group versus the OMT group for: The composite of death, myocardial infarction and stroke (20.0% versus 19.5%; hazard ratio 1.05 [95%CI: 0.87 – 1.27; P = 0.62]) Hospitalisation for acute coronary syndrome 12.4% versus 11.8%, HR 1.07(95%CI: 0.84 – 1.37; P = 0.56) Myocardial infarction 13.2% versus 12.3%, HR 1.13 (95%CI: 0.89 – 1.43; P = 0.33)</td>
</tr>
<tr>
<td>Study ID</td>
<td>N</td>
<td>Study design</td>
<td>Description - Participants and Interventions</td>
<td>Follow up (months)</td>
<td>Comments and results</td>
</tr>
<tr>
<td>----------</td>
<td>---</td>
<td>--------------</td>
<td>---------------------------------------------</td>
<td>------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Sedlis et al (2009)[12]</td>
<td>320 [149 – PCI + OMT group; 171 – OMT group]</td>
<td>Randomised controlled trial Multicentre, US &amp; Canada</td>
<td>Patients with myocardial ischemia and coronary artery disease and with chronic kidney disease (CKD) were compared with the rest of the cohort who did not have CKD. Percutaneous coronary intervention (PCI) with optimal medical therapy (OMT) versus OMT alone. Primary outcome: death from any cause and non-fatal myocardial infarction</td>
<td>4.6 years (median)</td>
<td>- CKD was found to be a significant independent predictor of death or nonfatal myocardial infarction Adjusted HR 1.48 (95%CI: 1.15 – 1.90; P = 0.002)  - PCI had no effect on death or non-fatal myocardial infarction in patients with or without CKD</td>
</tr>
<tr>
<td>Charytan et al (2009) [13]</td>
<td>5 studies with total 7,481 participants of which 1,453 classed as stages 3 to 5 CKD.</td>
<td>Systematic review and meta-analysis of randomised controlled trials.</td>
<td>Randomised trials including patients with non-ST ACS. Early angiography vs. symptom stress driven angiography and baseline eGFR. Required outcomes of mortality re-infarction, or re-hospitalisation and minimum 3 month follow-up.</td>
<td>Pooled results for 1-year outcomes for patients with Stage 3 to 5 CKD for invasive vs. conservative strategy:  - All-cause mortality: 0.76 (95%CI 0.49, 1.17).  - Non-fatal MI: 0.78 (95%CI 0.52, 1.16).  - Composite death and MI: 0.79 (95%CI 0.53, 1.18).  - Re-hospitalisation: 0.76 (95%CI 0.66, 0.87). Limitations: Meta-analysis undertaken for unplanned sub-groups from the original studies. eGFR based on baseline measurements. Trials conducted over a long time period i.e. &gt;10 years.</td>
<td></td>
</tr>
<tr>
<td>Halkin et al (2005) [15]</td>
<td>1314 CrCl (ml/min)  - ≤60 (223)  - 60-89 (419)  - ≥90 (658)</td>
<td>Sub group analysis of double blind placebo controlled randomised trial. Multi-centre (US)</td>
<td>Patients undergoing stenting of a single, de novo, coronary lesion. Exclusion included serum Cr &gt;2.0 mg/dL and significant comorbidities. Paclitaxel slow release stent vs. bare metal stent. Primary outcome: Rate of ischaemia driven target vessel revascularisation.</td>
<td>5 years</td>
<td>RR for group with CrCl ≤60 ml/min compared to &gt;60 ml/min.  - All-cause mortality at 1 year: 2.27 (95%CI 0.99,5.20) - control rate 1.6%  - Target vessel restenosis at 1 year: 0.82 (0.54, 1.24) – control rate 12.6% Limitations: Subgroup analysis of randomised trial. Serum Cr only available at baseline. Severe renal insufficiency excluded.</td>
</tr>
<tr>
<td>Study ID</td>
<td>N</td>
<td>Study design</td>
<td>Description - Participants and Interventions</td>
<td>Follow up (months)</td>
<td>Comments and results</td>
</tr>
<tr>
<td>------------------</td>
<td>-------</td>
<td>--------------------</td>
<td>-------------------------------------------------------------------------------------------------------------</td>
<td>-------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Sajja et al (2007) [17]</td>
<td>116</td>
<td>Open label randomised trials. Single centre (India)</td>
<td>Non dialysis dependent patients requiring primary CABG and with a GFR ≤60 ml/min/1.73m². On-pump vs. Off-pump bypass grafting. Primary outcome: Decline in preoperative GFR by 20% or more.</td>
<td>15 days</td>
<td>Relative risk following surgery in the off-pump group compared to the on-pump group: Increase in serum Cr by 20% or more: 0.47 (95%CI 0.30,0.72) control rate 62%. Increase in GFR by 20% or more: 0.55 (95%CI 0.35,0.87) control rate 55%. Patients requiring haemodialysis: 3/60 (5%) in on-pump group and 0/56 in the off-pump group. Mortality: 3/60 (5%) in on-pump group and 0/56 in the off-pump group with all deaths attributable to acute kidney injury. Limitations: Single centre study. No assessment of GFR beyond 5 days.</td>
</tr>
<tr>
<td>Gruberg et al (2003) [14]</td>
<td>1265</td>
<td>Retrospective review of medical records database. Single centre (US)</td>
<td>Consecutive patients who had undergone prior CABG. Excluded dialysis patients.</td>
<td>1 year</td>
<td>Procedural success similar between CrCl groups. All-cause mortality at 1 year for each CrCl group: &lt;30 ml/min: 36.7% (P&lt;0.001) 30-49 ml/min: 19.0% 50-69 ml/min: 8.0% ≥70 ml/min: 7.1% Multivariate logistic regression OR’s for independent predictors of late mortality: CrCl 50-69 ml/min: 0.19 (95%CI 0.07-0.55) CrCl ≥70 ml/min: 0.27 (95%CI 0.11-0.68) Limitations: Retrospective review of medical records. Single centre. Duration of renal insufficiency unknown. May not account for all comorbidities in survival analysis. CrCl available at baseline only.</td>
</tr>
<tr>
<td>Lok et al (2004) [16]</td>
<td>28,506</td>
<td>Retrospective review of medical records database. Multi-centre (Canada)</td>
<td>All patients who underwent CABG surgery from 1996 to 1999. Excluded dialysis patients.</td>
<td>1 year</td>
<td>Multivariate ORs for 30 day mortality: Serum Cr &lt;120: 1.0 Serum Cr 120-180: 1.6 (95%CI 1.2,2.1) Serum Cr &gt;180: 3.1 (95%CI 2.0-4.7). Control rate 1.7%. Multivariate ORs for 1 year mortality: Serum Cr &lt;120: 1.0 Serum Cr 120-180: 1.7 (95%CI 1.4,2.1) Serum Cr &gt;180: 3.4 (95%CI 2.5-4.8). Control rate 3.8%. Limitations: Retrospective review of medical records. Duration of renal insufficiency unknown. Serum creatinine used as marker for CKD as GFR was not able to be calculated and was available only at baseline.</td>
</tr>
<tr>
<td>Study ID</td>
<td>N</td>
<td>Study design</td>
<td>Description - Participants and Interventions</td>
<td>Follow up (months)</td>
<td>Comments and results</td>
</tr>
<tr>
<td>------------------</td>
<td>------</td>
<td>--------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------</td>
<td>-------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
• All-cause mortality from 30 days to 18.2 years after surgery: 1.44 (95%CI 1.06,1.96) (mortality in high eGFR group 45.2%).  
• Cardiac mortality from 30 days to 18.2 years after surgery: 1.51 (95%CI 1.04,2.19) (overall mortality in high eGFR group 38.6%). Limitations: Retrospective analysis of medical records from a single centre. Based on a Pre-operative measure of serum creatinine with no measure of change in renal function with time. |
| Cooper et al (2006) [19]    | 483,914 | eGFR (ml/min/1.73m²)  
• ≥90 (22%)  
• 60-89 (51%)  
• 30-59 (24%)  
• <30 (2%)  
• Dialysis (1.5%) | Retrospective analysis of medical records database:  
Multi-centre (US) | Patients receiving CABG from 2000 to 2003 with routine serum Cr measurement. Primary outcome: Operative mortality (death within 30 days of surgery). | 30 days | Adjusted ORs for operative mortality for relative to eGFR ≥90:  
• eGFR 89-60: 1.02 (95%CI 0.96,1.09)  
• eGFR 59-30: 1.55 (95%CI 1.45,1.65)  
• eGFR <30: 2.87 (95%CI 2.61,3.16)  
• Dialysis: 3.82 (95%CI 3.45,4.25). Control rate 1.3%. Limitations: Retrospective review. Likely excludes most severe cases as these are more likely to be medically managed. Renal function based on a single serum Cr. No data available on long-term survival. |
• HD: 27.7%  
• Non dialysis: 16.4% (P>0.05).  
• RR HD compared to non dialysis: 1.69 (95%CI 0.79,3.60) Limitations: Retrospective review of medical records. Single centre and small numbers. |
| Chonchol (2007) [21]        | 931  | eGFR (ml/min/1.73m²)  
• ≥60 (817)  
• <60 (114) | Retrospective analysis of medical records. Single centre (France) | Patients who underwent CABG between 1998 and 2002. Primary outcome: composite of death, acute coronary syndrome, stroke, revascularisation during follow-up. | 3.3 years (median) | Multivariate HRs for patients with eGFR <60:  
• Composite outcome: 1.46 (95%CI 1.01,2.11)  
• All-cause mortality: 1.89 (95%CI 1.16,3.07)  
• Cardiovascular mortality: not significant. Limitations: Retrospective review of medical records from a single centre. Cause and duration of CKD unknown. Baseline eGFR from a single serum Cr measurement. Medication use unknown. |
<table>
<thead>
<tr>
<th>Study ID</th>
<th>N</th>
<th>Study design</th>
<th>Description - Participants and Interventions</th>
<th>Follow up (months)</th>
<th>Comments and results</th>
</tr>
</thead>
</table>
| Hillis et al (2006) [22] | 2067       | Retrospective analysis of medical records. Single centre (Scotland) | Non dialysis patients who underwent CABG between 2000 and 2004. Primary outcome: Long-term all-cause mortality and 30 day all-cause mortality. | 2.3 years (median) | Adjusted HR for long term all-cause mortality relative to eGFR ≥75 with a mortality of 5%:  
  • <45: 1.83 (95%CI 1.04, 3.20)  
  • 45-59: 1.76 (95%CI 1.09, 2.86)  
  • 60-74: 1.00 (95%CI 0.61-1.64).  
 Adjusted HR for 30 day all-cause mortality relative to eGFR ≥75 with a mortality of 2%:  
  • <45: 2.11 (95%CI 0.79, 5.61)  
  • 45-59: 1.47 (95%CI 0.61, 3.53)  
  • 60-74: 0.70 (95%CI 0.27, 1.82).  
 Limitations: Retrospective review from a single centre. GFR based on single preoperative serum creatinine measurement. No information on non-fatal outcomes. Cause and duration of CKD unknown.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| Zakeri et al (2005) [23] | 4403       | Retrospective analysis of medical records. Multi centre (UK) | All patients undergoing isolated first time CABG with no history of renal disease or dialysis (serum Cr <2.26 mg/dL) between 1997 and 2004. Primary outcome: All-cause in hospital and long-term mortality. | 2.4 years (median) | Defined a reference group as having preoperative serum Cr<1.47 mg/dL (n=3945) and a renal group with serum Cr 1.47-2.25 mg/dL (n=458).  
 Multivariate OR for all cause in hospital death (rate 2.5%):  
  • Creatinine ≥130µmol/L: 1.91 (95%CI 1.16, 3.48)  
  • GFR <60 ml/min/1.73m²: 1.98 (95%CI 1.16,3.48)  
 Multivariate OR for all-cause long-term mortality (rate 13%):  
  • Creatinine ≥130µmol/L: 1.65 (95%CI 1.25,2.18)  
  • GFR <60 ml/min/1.73m²: 1.56 (95%CI 1.14,2.13)  
 Limitations: Retrospective review. Renal function based on single serum creatinine measurement. Cause of death unknown. No knowledge of cause or duration of CKD.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Gajdos et al (2013)[24] | 1409 (ESRD) 34,813 (non-ESRD) | Retrospective data analysis. US | Patients with end-stage renal disease (ESRD) undergoing major elective vascular surgery. Primary outcomes: postoperative complications and death | 1 |  
  • ESRD patients compared to the non-ESRD group, had greater rate of overall complications 16.5% versus 8.4% (P<0.001); death 7.2% versus 1.4%. (P<0.001); and return to the operating room 23.8% versus 8.5%, (P<0.001).  
  • Patients with ESRD were significantly more likely to develop surgical site infection Adj Odds Ratio 1.54 (95%CI: 1.22 – 1.93), unplanned intubation OR adj 2.07 (95%CI: 1.56 – 2.74), ventilator dependence OR adj 1.61 (95%CI: 1.21 – 2.14), a return to the operating room OR adj 2.11 (95%CI: 1.83 – 2.44), and death within 30 days of operation OR adj 4.46 (95%CI: 3.48 – 5.72) as compared with non-ESRD patients.  
  • Older ESRD patients were more likely to have unplanned intubation, odds ratio (OR) 1.84, (95%CI: 1.07 – 3.16); worse combined pulmonary outcome OR 1.61 (95%CI: 1.08 – 2.41); and post-operative death OR 1.75 (95%CI: 1.12 – 2.73) compared with younger ESRD patients.  
<p>| Outcomes of revascularisation: coronary artery bypass grafting and dialysis |</p>
<table>
<thead>
<tr>
<th>Study ID</th>
<th>N</th>
<th>Study design</th>
<th>Description - Participants and Interventions</th>
<th>Follow up (months)</th>
<th>Comments and results</th>
</tr>
</thead>
</table>
  - Dialysis patients - 13.8% (9/65).  
  - All cardiac patients during same time period – 3.4%.  
  Limitations: Retrospective review. Small numbers. Single centre. Control group not defined and level of matching unknown.                                                                                                         |
| Krabatsch et al (2005)    | 71     | Retrospective analysis of medical records.                                   | All HD patients who underwent CAPBG between 2001 and 2004. Control group (1:1) randomly selected from non dialysis cardiac patients. | NA                | HD CAPB patients represented 1.12% of total CABG patients. Perioperative mortality:  
  - Dialysis patients – 5.6% (4/71).  
  - Control group – 2.9% (2/68).  
  1 year survival:  
    - Dialysis patients – 88%.  
    - Control group – 91%.  
  4 year survival:  
    - Dialysis patients – 88%.  
    - Control group – 57%.  
 Limitations: Retrospective review. Small numbers. Single centre. Control group poorly defined unable to assess level of matching. |
  - Dialysis 9%, control group 6% (OR: 1.16, 95%CI 0.55,2.47).  
  Requirement for blood transfusions:  
    - Dialysis 23%, control group 77% (OR: 11.39, 95%CI 5.80,29.94).  
 Limitations: Retrospective review. Small numbers. Single centre. Control group poorly defined unable to assess level of matching. |
| Herzog et al (1999) [28]  | 14,306 | Retrospective review of population based medical registry (US).              | Dialysis patients hospitalised for the first coronary revascularisation by PTCA or CAB surgery and who received dialysis for at least 60 days prior to revascularisation over the period 1978 to 1995. | Mean 1.59 years for PTCA and 1.88 years for CAB. | Survival similar between CABG and PTCA.  
  1 year event free survival (all-cause death):  
    - CABG – 70.6% (sd 43.1%)  
  2 year event free survival (all-cause death):  
    - CABG – 56.9% (sd 60.3%)  
  5 year event free survival (all-cause death):  
    - CABG – 26.5% (sd 69%)  
 Limitations: Retrospective review of registry which contains little clinical data. No control. |

Cardiovascular Disease  May 2013  Page 14 of 25
<table>
<thead>
<tr>
<th>Study ID</th>
<th>N</th>
<th>Study design</th>
<th>Description - Participants and Interventions</th>
<th>Follow up (months)</th>
<th>Comments and results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herzog et al (2002) [29]</td>
<td>15,784</td>
<td>Retrospective review of population based medical registry (US).</td>
<td>Dialysis patients hospitalised for the first coronary revascularisation by PTCA or CAB surgery or coronary artery stenting and who received dialysis for at least 60 days prior to revascularisation over the period 1995 to 1998.</td>
<td>Mean 18.3 months for PTCA and 17.6 months for CAB and 13.3 months for stents.</td>
<td>In hospital death 12 month event free survival (all-cause death): • CABG – 71.5% (sd 90%) 2 year event free survival (all-cause death): • CABG – 56.4% (sd 114%) 3.5 year event free survival (all-cause death): • CABG – 37.0% (sd 139%) Limitations: Retrospective review of registry which contains little clinical data. No control.</td>
</tr>
<tr>
<td>Herzog et al (2004) [31]</td>
<td>2,661</td>
<td>Retrospective review of population based medical registry (US).</td>
<td>Kidney transplant recipients who have undergone coronary revascularisation during the period 1995 to 1999.</td>
<td>Mean 31.9 months for PTCA and 24.8 months for CAB and 21.3 months for stents.</td>
<td>12 month event free survival (all-cause death): • CABG (IMG-) – 79.6% (sd 83.1%) • CABG (IMG+) – 87.3% (sd 67.1%) 2 year event free survival (all-cause death): • CABG – 74.4% (sd 92%) • CABG (IMG+) – 82.7% (sd 81%) 4 year event free survival (all-cause death): • CABG – 68.4% (sd 117%) • CABG (IMG+) – 67.2% (sd 137%) Limitations: Retrospective review of registry which contains little clinical data. No control.</td>
</tr>
<tr>
<td>Naidu et al (2003) [32]</td>
<td>4,602</td>
<td>Retrospective review of medical registry. Multi-centre (US).</td>
<td>Patients who underwent PCI during between 1997 and 1998 and in 1999. Renal disease defined as increased creatinine level with a history of renal failure treated with medication, dialysis or low protein diet.</td>
<td>NA</td>
<td>Mean CrCl ml/min: • Renal disease 40.3±28.4 • No renal disease 96.2±36.0 Adjusted OR’s for renal disease vs. no renal disease: • In hospital all-cause mortality: 3.8 (95%CI 1.7-8.6). Control rate 1.2%. • 1 year all-cause mortality: 2.5 (95%CI 1.6-3.7). Control rate 4.4%. Limitations: Retrospective review of medical registry. Renal function assessed on basis of one measure of serum creatinine.</td>
</tr>
<tr>
<td>Study ID</td>
<td>N</td>
<td>Study design</td>
<td>Description - Participants and Interventions</td>
<td>Follow up (months)</td>
<td>Comments and results</td>
</tr>
<tr>
<td>---------</td>
<td>---</td>
<td>--------------</td>
<td>-----------------------------------------------</td>
<td>-------------------</td>
<td>---------------------</td>
</tr>
</tbody>
</table>
| Best et al (2002) [33] | 5,327 | CrCl (ml/min) ● <30 (154) ● 30-49 (899) ● 50-69 (1,537) ● ≥70 (2,687) ● Dialysis (50) | Retrospective review of medical registry. Single centre (US-Mayo Clinic). All patients undergoing PCI during 1994 and 1999. | NA | Multivariate estimated risk ratios for all-cause mortality relative to the CrCl quadratic of 90 ml/min:  
- 70 ml/min: 1.46 (95%CI 1.3,1.6)  
- 50 ml/min: 2.25 (95%CI 1.8,2.9)  
- 30 ml/min: 3.70 (95%CI 2.5,5.5)  
- Dialysis: 8.91 (95%CI 5.3,15.0).  
Limitations: retrospective review of medical registry. Renal function assessed on basis of one measure of serum creatinine. |
| Zheng et al (2012)[34] | 9838 | Retrospective data analysis Coronary Artery Bypass Grafting Registry China | Patients undergoing coronary artery bypass grafting (CABG) Primary outcome: risk factors for in-hospital mortality | N/A | The mortality rate for isolated-CABG was 2.0%, this increased to 6.3% when CABG was combined with valve procedures.  
Chronic renal failure odds ratio 2.40 (95%CI: 1.27 – 4.53; P=0.007 along with 10 other risk factors were identified as being associated with in-hospital mortality for patients undergoing CABG. |
| Sadeghi et al (2003) [35] | 2082 | CrCl (ml/min) ● ≤60 (350) ● >60 (1583) | Sub group analysis of open label randomised controlled trial. Multi-centre (International) | 12 | RR in ≤60 ml/min group compared to >60 ml/min group:  
- All-cause mortality at 1 year – 5.3 (95%CI 3.5,8.1) – control rate 2.4%  
- Cardiovascular mortality at 1 year – 6.0 (95%CI 3.4,10.7) – control rate 1.2%  
- Target vessel revascularisation at 1 year – 0.9 (95%CI 0.7,1.2) – control rate 13.8%  
Severe restenosis:  
- ≤60 ml/min - 26.5% in PTCA and 15.1% in stent groups (P=0.15)  
- >60 ml/min – 17.6% in PTCA and 6.1% in stent groups (P<0.0001)  
Limitations: Subgroup analysis of randomised trial. Serum Cr only available at baseline. Small proportion of low CrCl. |
<table>
<thead>
<tr>
<th>Study ID</th>
<th>N</th>
<th>Study design</th>
<th>Description - Participants and Interventions</th>
<th>Follow up (months)</th>
<th>Comments and results</th>
</tr>
</thead>
</table>
  - Dialysis: 2.8 (95%CI 0.9,9.2)  
  - Chronic renal failure: 2.7 (95%CI 1.4,5.1)  
Multivariate estimated risk ratios for all-cause mortality:  
  - Dialysis: 2.6 (95%CI 0.9,7.4)  
  - Chronic renal failure: 3.0 (95%CI 1.7,5.1)  
  
  All-cause mortality in CRF:  
  - 1 year 16%  
  - 2 year 30%  
  
  Limitations: retrospective review of medical registry. Renal function assessed on basis of one measure of serum creatinine. |
| Reinecke et al (2003) [37] | 1,049 | Serum Cr (mg/dL) ≤1 (437)  
  1.1-1.2 (386)  
  1.3-1.4 (132)  
  1.5-2.0 (55)  
  >2.0 (39) | Retrospective review of medical registry. Single centre (Germany). All patients undergoing PCI during 1998 to 1999. | 3.2 years | 30 day all-cause mortality by serum Cr grouping (mg/dL):  
  ≤1: 1.1%  
  1.1-1.2: 1.8%  
  1.3-1.4: 0.8%  
  1.5-2.0: 11.1% (P<0.001)  
  >2.0: 10.3% (P<0.001)  
All-cause mortality at follow-up by serum Cr grouping (mg/dL):  
  ≤1: 5.5%  
  1.1-1.2: 7.8%  
  1.3-1.4: 12.1% (P<0.05)  
  1.5-2.0: 25.5% (P<0.001)  
  >2.0: 30.8% (P<0.001)  
  
  Limitations: retrospective review of medical registry. Renal function assessed on basis of one measure of serum creatinine. |
  - CKD: 10.8%  
  - Non CKD: 1.1% P<0.0001  
1 year event free survival:  
  - CKD: 55% (95%CI: 49,61)  
  - Non CKD: 78% (95%CI: 71,84) P<0.0001.  
  
  Limitations: retrospective review of medical registry. Renal function assessed on basis of one measure of serum creatinine. |

**Percutaneous coronary intervention: dialysis**
<table>
<thead>
<tr>
<th>Study ID</th>
<th>N</th>
<th>Study design</th>
<th>Description - Participants and Interventions</th>
<th>Follow up (months)</th>
<th>Comments and results</th>
</tr>
</thead>
</table>
| Schoebel et al (1997) [40] | 40 | Retrospective case control. Single centre (Germany) | ESRD patients who had undergone first elective and primarily successful PTCA. Control were age and sex matched randomly selected PTCA patients. | Not stated | Odds ratio of clinical restenosis:  
- 3.45 (95% CI 0.84, 12.65)  
Limitations: Retrospective assessment. Small numbers. Single centre. No patient important outcomes (e.g. death, CVD events). Cases higher number of risk factors than controls. |
| Kahn et al (1990) [41] | 17 | Retrospective review of medical records. Single centre (US) | Dialysis patients treated with PTCA. | 20 months (mean) | Rate of restenosis:  
- 26 of 32 dilated zones or 81% restenosis.  
| Wimmer et al (2012)[42] [SAPPHIRE Study] | 10,186 | Analysis and Model prediction Multicentre: US & Canada. | Patients with carotid stenosis undergoing carotid artery stenting (CAS). Patients with at least one factor (anatomic or comorbid) that made them high risk for carotid endarterectomy were included. | NA | - Within 30 days of coronary artery stenting, death occurred in 123 patients (1.2%) and stroke in 301 patients (3.0%).  
- Stroke or death within 30 days occurred in 366 patients (3.6%)  
- There were 10 significant predictors for death or stroke within 30 days after CAS being on dialysis increased this risk (odds ratio adj 2.68 [95% CI: 1.34 – 6.01; P<0.007)  
Outcomes of coronary artery stenting: chronic kidney disease  
Lemos et al (2005) [43] | Normal renal function:  
- Bare stent (451)  
- SES (443)  
Renal impairment (CrCl <60 ml/min):  
- Bare stent (92)  
- SES (94) | Retrospective review of medical records with historical controls. Single centre (Brazil) | Patients treated with Sirolimus Eluting Stents (SES). Historical controls selected from patients treated with bare metal stents prior to adoption of SES. | 1 year | HRs for all-cause mortality at 1 year:  
- Total population:  
  - Renal impairment vs normal: 3.14 (95% CI 1.68, 5.88). Control rate 2.5%  
- Bare metal stents  
  - Renal impairment vs normal: 2.68 (95% CI 1.07, 6.73). Control rate 2.5%  
- SES  
  - Renal impairment vs normal: 3.60 (95% CI 1.52, 8.54). Control rate 3.2%  
Adjusted HR for 1 year all-cause mortality:  
- Renal impairment 2.15 (95% CI 1.10,4.28)  
- SES use 1.10 (95% CI 0.59,2.07)  
Adjusted 1 year target vessel revascularisation rate:  
- Renal impairment 1.22 (95% CI 0.79,1.88)  
- SES use 0.43 (95% CI 0.29,0.64)  
<table>
<thead>
<tr>
<th>Study ID</th>
<th>N</th>
<th>Study design</th>
<th>Description - Participants and Interventions</th>
<th>Follow up (months)</th>
<th>Comments and results</th>
</tr>
</thead>
</table>
| Marzocchi et al (2007) [44] |    | ● Bare stent (7565) ● DES (3064)                   | Retrospective review of registry database (REAL). Multi-centre (Italy) All patients treated with either a bare metal or drug eluting stent (DES) between 2002 and 2005. | 23 (mean)        | Adjusted HR for 2 year target vessel restenosis:  
  • Renal failure: 1.69 (95%CI 1.06-2.68) (control rate 13%)  
  • DES: 0.75 (95%CI 0.64-0.88) (control rate 13%)  
  Limitations: Retrospective assessment. Number of significant differences between bare metal and DES patients at baseline. No assessment of CKD on patient important outcomes e.g. mortality and CVD events. |
| Pinkau et al (2004) [45]   | 4,131 | ● Stent (3,181) ● Angioplasty (950) ● CrCl <60 ml/min (1,412) | Retrospective review of medical records. Single centre (Germany) Patients who underwent PTCA or stenting between 1996 and 2001. Excluded patients with ESRD. | 12                | Unadjusted HRs CrCl <60 ml/min vs. ≥60 ml/min:  
  • Restenosis: 1.15 (95%CI 0.97,1.36). Control rate 30%.  
  • All-cause death at 1 year: 3.72 (95%CI: 2.65,5.22). Control rate 2%.  
  Limitations: Retrospective assessment. CrCl based on single serum Cr at baseline. No breakdown between PTCA and stents. |
| Charytan et al (2011) [46] | 1,749 | ● BMS (493) ● DES with CRF (1,256)                  | Retrospective review of medical register. Multi-centre (US) All adults (≥18 years) who underwent PCI with stent emplacement and recorded as having severely decreased GFR. Excluding those who received both BMS and DES. Comparison of patients treated with BMS and DES. Primary outcome: All-cause mortality at 2 years. | 2 years           | Overall 24% of patients classed as having severely decreased GFR were on dialysis. Unadjusted risk ratios for patients recorded as having severely decreased GFR treated with DES compared to BMS:  
  • All-cause mortality: 0.76 (95%CI 0.66, 0.87).  
  • MI : 0.79 (95%CI 0.63, 0.99).  
  • TVR : 0.78 (95%CI 0.61, 0.99).  
  Risk ratios for ‘matched’ patients with severely decreased GFR and treated with DES compared to BMS:  
  • All-cause mortality: 1.06 (95%CI 0.89, 1.25).  
  • MI : 0.84 (95%CI 0.63, 1.13).  
  • TVR : 0.74 (95%CI 0.54, 1.10).  
  Limitations: Retrospective review of medical register. Differences between DES and BMS groups at baseline. No record of serum creatinine with ‘Severely decreased GFR’ based on record entry in data base. |
<table>
<thead>
<tr>
<th>Study ID</th>
<th>N</th>
<th>Study design</th>
<th>Description - Participants and Interventions</th>
<th>Follow up (months)</th>
<th>Comments and results</th>
</tr>
</thead>
</table>
Comparison of patients with low and normal eGFR treated with BMS and DES.  
Outcomes: All-cause mortality, MI, repeat PCI at 1 year. | 1 year | Adjusted hazard ratios for DES compared to BMS in patients with low eGFR.  
• All-cause mortality: 1.05 (95%CI 0.59, 1.85).  
• MI: 0.88 (95%CI 0.51, 1.54).  
• Repeat PCI: 0.63 (95%CI 0.40, 1.01).  
Limitations: Retrospective review of register. Excluded dialysis patients. Some differences in baseline characteristics between DES and BMS patients. GFR defined by single serum creatinine measurement at baseline. |
| Kersting et al (2012) [48]           | 1,184 | Retrospective review of medical register. | Consecutive patients who underwent PCI with eGFR <60 ml/min. Excluded patients with no serum creatinine at baseline and who had unknown or both DES and BMS.  
Comparison of BMS and DES.  
Primary outcome: All-cause mortality. | Mean 2.8 years. | Unadjusted risk ratio for patients with eGFR <60 ml/min compared to patients with eGFR ≥60 ml/min:  
• All-cause mortality: 2.82 (95%CI: 2.09, 3.79)  
• MI: 2.05 (95%CI: 1.37, 3.08)  
• Stent thrombosis: 1.91 (95%CI: 1.89, 2.87)  
Unadjusted risk ratio for patients with eGFR <60 ml/min treated with DES compared to patients with eGFR <60 ml/min treated with DES:  
• All-cause mortality: 0.42 (95%CI: 0.28, 0.70)  
• MI: 0.97 (95%CI: 0.48, 1.97)  
Adjusted hazard ratios for patients with eGFR <60 ml/min treated with DES compared to patients with eGFR <60 ml/min treated with DES:  
• All-cause mortality: 1.03 (95%CI: 0.51, 2.32)  
• MI: 0.34 (95%CI: 0.10, 1.12)  
• Stent thrombosis: 0.79 (95%CI: 0.21, 2.99)  
Limitations: Retrospective review of registry at a single centre. eGFR estimated on single serum creatinine at baseline. Choice of DES/BMS subject to clinician preferences. |
<table>
<thead>
<tr>
<th>Study ID</th>
<th>N</th>
<th>Study design</th>
<th>Description - Participants and Interventions</th>
<th>Follow up (months)</th>
<th>Comments and results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tsai et al (2011). [49]</td>
<td>283,593</td>
<td>Retrospective review of medical registers. Multi-centre (US)</td>
<td>All Medicare-eligible patients ≥65 years of age who underwent PCI. Excluded those missing serum creatinine not on dialysis and treated with both BMS and DES. Comparison of BMS and DES. Primary outcomes: all-cause mortality, MI, repeat PCI, follow-up bleeding.</td>
<td>30 months</td>
<td>Adjusted hazard ratio for patients with eGFR &lt;60 ml/min compared to patients with eGFR ≥60 ml/min:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• All-cause mortality:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: 45-59: 1.11 (95%CI: 1.08, 1.15)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: 30-44: 1.45 (95%CI: 1.40, 1.51)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: &lt;30: 1.87 (95%CI: 1.76, 1.98)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o Dialysis: 3.55 (95%CI: 3.36, 3.74)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• MI:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: 45-59: 1.06 (95%CI: 1.01, 1.11)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: 30-44: 1.14 (95%CI: 1.07, 1.20)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: &lt;30: 1.34 (95%CI: 1.21, 1.49)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o Dialysis: 2.11 (95%CI: 1.91, 2.31)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Revascularisation:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: 45-59: 0.72 (95%CI: 0.68, 0.77)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: 30-44: 0.73 (95%CI: 0.68, 0.79)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: &lt;30: 0.90 (95%CI: 0.79, 0.97)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o Dialysis: 1.13 (95%CI: 1.04, 1.23)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Odds ratios for patients (propensity matched) treated with DES compared to BMS:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• All-cause mortality:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: ≥60: 0.72 (95%CI: 0.68, 0.76)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: 45-59: 0.73 (95%CI: 0.68, 0.79)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: 30-44: 0.73 (95%CI: 0.68, 0.79)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: &lt;30: 0.90 (95%CI: 0.79, 0.97)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o Dialysis: 0.88 (95%CI: 0.77, 1.00)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• MI:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: ≥60: 0.72 (95%CI: 0.67, 0.78)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: 45-59: 0.74 (95%CI: 0.65, 0.83)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: 30-44: 0.82 (95%CI: 0.71, 0.95)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: &lt;30: 0.75 (95%CI: 0.58, 0.97)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o Dialysis: 0.76 (95%CI: 0.71, 0.80)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Revascularisation:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: ≥60: 0.91 (95%CI: 0.87, 0.95)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: 45-59: 0.96 (95%CI: 0.88, 1.01)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: 30-44: 1.01 (95%CI: 0.91, 1.11)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o eGFR: &lt;30: 1.02 (95%CI: 0.97, 1.07)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>o Dialysis: 1.01 (95%CI: 0.80, 1.27)</td>
</tr>
</tbody>
</table>

Limitations: retrospective review of registry data. eGFR based on serum creatinine at baseline. Clinician determined treatment.

Outcomes of coronary artery stenting: dialysis
<table>
<thead>
<tr>
<th>Study ID</th>
<th>N</th>
<th>Study design</th>
<th>Description - Participants and Interventions</th>
<th>Follow up (months)</th>
<th>Comments and results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdel-Latif (2010) [50]</td>
<td>7 non-randomised studies (869 participants)</td>
<td>Systematic review and meta-analysis of non-randomised controlled studies.</td>
<td>Non-randomised controlled trials of ESRD patients comparing drug eluting stents (DES) with bare metal stents (BMS).</td>
<td>Range 9 to 36 (median 12).</td>
<td>Sample size range 54-204 (median 108). Risk of all-cause mortality in patients receiving DES compared to BMS: OR: 0.68 (0.45,1.01) BMS rate 18%. Risk of target lesion or target vessel revascularisation in patients receiving DES compared to BMS: OR: 0.55 (0.39,0.79) BMS rate 25%. Risk of major adverse clinical event in patients receiving DES compared to BMS: OR: 0.54 (0.40,0.73) BMS rate 40%. Limitations: Meta-analysis of non-randomised trials non blinded studies and thus subject to both selection and allocation bias. Small studies.</td>
</tr>
<tr>
<td>Ishii et al (2012) [51]</td>
<td>505</td>
<td>Retrospective review of medical records. Single-centre (Japan)</td>
<td>Haemodialysis patients who underwent first PCI with stenting. Excluded patients with cancer and CABG. Comparison of BMS with DES. Outcomes: MACE (all-cause death, cardiac death, MI, stent thrombosis and TLR).</td>
<td>Mean 42±30 months – BMS. Mean 30±18 months – DES.</td>
<td>Unadjusted risk ratio for patients treated with DES compared to patients treated with BMS: All-cause mortality: 0.63 (95%CI: 0.49, 0.83) MI: 0.93 (95%CI: 0.38, 2.28) Stent thrombosis: 1.19 (95%CI: 0.35, 4.00) TLR: 0.69 (95%CI: 0.53, 0.89) The 6 year mortality rates for all-cause death were comparable between BMS and DES at 42.1 and 36.7% (P=0.88) respectively. Limitations: Retrospective review of medical records in a single centre. DES or BMS treatment determined by clinician. Differing follow-up periods between BMS and DES groups.</td>
</tr>
<tr>
<td>Ikari et al (2012) [56]</td>
<td>117</td>
<td>Prospective cohort. Multi centre (Japan)</td>
<td>Adult (≥21 years) haemodialysis patients who underwent PCI with a Sirolimus Eluting Stent (SES). Primary outcomes: Target vessel failure (TVF) (composite of cardiac death, MI in the target vessel, and TVR) within 1 year</td>
<td>1 year.</td>
<td>Loss to follow up 2.5%. Cohort consisted of: Male: 69%. Age: 65.0±10.4 years DM 70%. Previous PCI: 31%. One year outcomes: All-cause mortality 9.4%. Cardiac death: 2.6%. MI: 1.4%. Stent thrombosis: 0.9%. TLR: 22.2%. Limitations: Observational study. No non-dialysis control group. No BMS comparison group.</td>
</tr>
<tr>
<td>Study ID</td>
<td>N</td>
<td>Study design</td>
<td>Description - Participants and Interventions</td>
<td>Follow up (months)</td>
<td>Comments and results</td>
</tr>
<tr>
<td>----------</td>
<td>----</td>
<td>--------------</td>
<td>---------------------------------------------</td>
<td>-------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Sakakibara et al (2012) [57]</td>
<td>100</td>
<td>Open label randomised controlled clinical trial Single centre (Japan)</td>
<td>Prospective maintenance HD patients with stable angina pectoris who underwent PCI for native coronary lesions. Sirolomus eluting stent (SES) vs. everolimus eluting stent (EES). Primary outcome: rate of restenosis at 8 months. Secondary outcomes, composite endpoint of major adverse events after PCI (all-cause death, nonfatal MI, target lesion revasc.).</td>
<td>8 months.</td>
<td>Risk ratio for lesion restenosis in EES group compared to SES: 0.41 (95%CI: 0.17, 1.00). Calculated on the basis of number of lesions in each group as number of patients affected by restenosis has not been provided. Rate of restenosis in SES group 14 per 66 lesions (8.7%). Risk ratio and risk difference for composite adverse event endpoint in EES group compared to SES: RR: 2.20 (95%CI: 0.82, 5.87). Rate of composite adverse event endpoint in SES group 22%. RD 0.12 (95%CI: -0.02, 0.26). Limitations: Single centre study. Open label. No details provided on treatment allocation or assessor blinding. No sample size calculation.</td>
</tr>
<tr>
<td>Study ID (author, year)</td>
<td>Method of allocation concealment *</td>
<td>Blinding (participants)</td>
<td>Blinding (investigators)</td>
<td>Blinding (outcome assessors)</td>
<td>Intention-to-treat analysis †</td>
</tr>
<tr>
<td>------------------------</td>
<td>--------------------------------</td>
<td>-------------------------</td>
<td>--------------------------</td>
<td>----------------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Manske et al 1992 [9]</td>
<td>Not specified</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>McFalls et al (2004) [10]</td>
<td>Stratified with permuted blocks</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Boden et al (2007) [11]</td>
<td>Permuted blocks and stratified</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Sadeghi et al (2003) [35] (see [58])</td>
<td>Not specified</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Halkin et al (2005) [15] (see [59])</td>
<td>Central</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Sajja et al (2007) [17]</td>
<td>Computer generated random number table</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Figure 1. Trail profile for the FRISC II trial.