Is standardized cardiac assessment of asymptomatic high-risk renal transplant candidates beneficial?

Jeroen Aalten¹, Stijn A. Peeters¹, Maureen J. van der Vlugt² and Andries J. Hoitsma¹

¹Department of Nephrology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands and ²Department of Cardiology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Abstract

Background. Perioperative cardiovascular events in renal transplantation are common and non-invasive cardiac stress tests are recommended in high-risk renal transplant candidates. In 2004, we introduced a standardized preoperative cardiac risk assessment programme with the aim of reducing perioperative cardiac events.

Methods. Since 2004, all asymptomatic high-risk renal transplant candidates had to undergo non-invasive cardiac stress testing. Patients with a positive stress test went for a coronary angiography and if indicated for revascularization. The incidence of perioperative cardiac events (≤30 days of transplantation) was analysed in all high-risk patients who received a transplantation (screening group) and compared with high-risk renal transplant recipients evaluated in the 4 years before the introduction of the cardiac assessment programme (historical control group).

Results. Since 2004, 227 of 349 asymptomatic high-risk renal transplant candidates underwent non-invasive cardiac stress testing. In 15 patients (6.6%), significant ischaemia was found. Ten of these 15 patients underwent coronary angiography (eight patients had significant coronary artery disease and in five patients, percutaneous coronary intervention was performed). One hundred and sixty of 349 renal transplant candidates have received renal transplantation so far (screening group). In the screening group, 6 perioperative cardiac events (3.8%) occurred compared to 13 perioperative events (7.6%) in the historical control group (n = 172) (P = 0.136).

Conclusions. The incidence of significant cardiac ischaemia in high-risk renal transplant patients was low and was followed by revascularization in a small percentage of patients. No significant decrease in perioperative cardiac events was observed after the introduction of the standardized cardiac assessment programme.

Keywords: cardiac events; cardiac risk assessment; non-invasive cardiac stress testing; renal transplantation; revascularization

Introduction

Renal transplantation is the preferred treatment option for most patients with end-stage renal disease (ESRD). Since the first transplantation, results have improved substantially [1, 2]. In most transplant centres, graft survival in the first year is between 90 and 95% [3]. With this high success rate, the acceptance rate for renal transplantation has been extended. Patients with obesity, older age and a history of cardiovascular events are now accepted for renal transplantation [4]. This extension of acceptance may lead to an increase of perioperative cardiac events and death after transplantation. Humar et al. [5] found an incidence of cardiac complications (including arrhythmia and congestive heart failure) of 6.1% in the first 30 days after transplantation. In recent studies, the incidence of myocardial infarction in the first year after transplantation was ~3.5 to 5%, with the highest incidence in the first 3 months after transplantation [6-8].

Although the prevalence of coronary artery disease at the time of renal transplantation is high, many renal transplant candidates are asymptomatic [6, 9-11]. Several international guidelines therefore recommend evaluation of asymptomatic high-risk renal transplant candidates with stress perfusion (myocardial scintigraphy) or dobutamine stress echocardiogram or coronary angiography and to perform an intervention in case of significant coronary artery disease [12, 13]. There is no evidence that this policy reduces the incidence of perioperative cardiac events in renal transplantation. Recent publications even doubt the benefit of preoperative revascularization [14-17].

In the beginning of 2004, we introduced a protocol for the preoperative cardiac assessment of all asymptomatic high-risk renal transplant candidates in our hospital to assess significant cardiac ischaemia with non-invasive cardiac stress testing. The protocol was based on international guidelines [12, 13, 18]. The aim of this study is to evaluate the effect of standardized cardiac assessment on the incidence of perioperative cardiac events; wherefore, we compared the incidence of perioperative cardiac events in high-risk renal transplant recipients evaluated...
before and after the introduction of the standardized protocol.

Materials and methods

In our region, all renal transplant candidates, without a clear contraindication, are referred for evaluation to the outpatient clinic of the University Medical Centre by their treating nephrologist. In January 2004, we introduced a standardized protocol for preoperative cardiac risk assessment of renal transplant candidates. In this protocol, all asymptomatic renal transplant candidates were screened for six clinical risk factors: age ($\geq$ 45 years for men and $\geq$ 55 years for women), diabetes, current smoker, cardiovascular history [acute coronary syndrome (ACS), percutaneous coronary intervention (PCI), coronary artery bypass grafting (CAG)], cerebrovascular accident, transient ischaemic attack, heart valve operation, heart failure, peripheral arterial disease], an abnormal electrocardiography (ECG) (except left ventricular hypertrophy) and obesity (body mass index $\geq$ 30 kg/m$^2$) [7, 8, 18–20]. Patients with $\geq$ one risk factor were classified as high-risk patients. All other patients (with no risk factors) were classified as low-risk patients. In all high-risk patients, non-invasive cardiac stress testing had to be performed for further risk stratification [physiologically or pharmacologically (adenosine or dobutamine) induced stress perfusion with myocardial scintigraphy or dobutamine stress echocardiography]. In most patients, the non-invasive cardiac stress test was performed in the general hospital. The type of stress test was dependent on the experience in the general hospital. Dobutamine stress echocardiography was only performed in the University Medical Hospital. A non-invasive cardiac stress test was considered positive if two or more myocardial segments (17-segment scheme) showed stress-induced ischaemia. Patients with a positive non-invasive cardiac stress test went for coronary angiography. Significant coronary artery disease was defined as a coronary artery stenosis of $>70\%$. All patients with significant coronary artery disease were referred for intervention. The final decision for intervention (PCI or CAG) was left to the treating cardiologist. All interventions were done in the University Medical Centre. The final decision on whether patients were accepted for renal transplantation was made by the transplant team.

Before 2004, non-invasive cardiac stress testing was not performed on a routine basis but driven by the treating physician (cardiologist or nephrologist). These non-invasive cardiac stress tests were not often performed at that time, only in patients with diabetic nephropathy or with a history of cardiovascular disease.

 Patients and study groups

We retrospectively collected the data from all adult renal transplant candidates who were evaluated in our outpatient clinic for kidney transplantation between 1 January 2004 and 19 May 2008 (screening group). Patients with angina [New York Heart Association functional class > 1 ($n = 211$)] were excluded from this data analysis.

For all asymptomatic transplant candidates, we assessed the clinical risk score. All asymptomatic patients were included in this study and all data concerning non-invasive cardiac stress testing, coronary angiographies, revascularization, wait-listing, renal transplantation and perioperative cardiac events were collected from the medical file. In our study, we did not collect data about preoperative cardiac events (cardiac events between non-invasive cardiac stress testing and transplantation).

Historical control group. To analyse if the incidence of perioperative cardiac events decreased after the introduction of our standardized cardiac assessment protocol, we made a comparison with a historical control group. For the historical control group, we collected data from all adult asymptomatic renal transplant candidates that were evaluated at our outpatient clinic during the 4 years before the introduction of our cardiac assessment programme (from 2000 to 2004) and received a renal transplantation. These patients were retrospectively divided into a low-risk group and high-risk group, based on the previously given definition.

Definition of perioperative cardiac events. A perioperative event was defined as the composite end point of any cardiac event within 30 days after transplantation including cardiac death, ACS [ST-elevation myocardial infarction (STEMI); non-STEMI or unstable angina], PCI and CAG. A STEMI was defined as at least 1 mm (0.1 mV) of ST-segment elevation in two limb leads and at least 2 mm ST elevation in two consecutive precordial leads. Non-STEMI was defined as an ECG without ST elevation but with elevated troponins ($\geq$ 0.2 $\mu$g/L) $>6$ h after cardiac complaints. For further analysis, we grouped the cardiac events in major (cardiac death, STEMI, non-STEMI with peak troponin $\geq$ 3 $\mu$g/L or intervention) and minor cardiac events (non-STEMI with peak troponin $<3$ $\mu$g/L).

End points of the study.

Cardiac evaluation in high-risk renal transplant candidates:
- The incidence of significant cardiac ischaemia
- The incidence of significant coronary artery disease
- The incidence of coronary interventions (PCI/CAG)
- The influence of screening on evaluation time and wait-listing

Perioperative cardiac events after renal transplantation:
- The incidence of perioperative cardiac events in high-risk renal transplant candidates
- The incidence of perioperative cardiac events before and after the introduction of the cardiac evaluation programme.

Statistical analyses

Statistical analysis was performed with SPSS 16.0. Patient characteristics of the different groups were compared using the Pearson’s chi-square test or the Fisher’s exact test for categorical data and the Student’s t-test or the Mann–Whitney U-test for continuous data. We compared the incidence of perioperative cardiac events between the screening and the historical control group. A P-value of $<0.05$ (two sided) was considered significant.

Results

Cardiac evaluation

Between 2004 and 2008, we evaluated 466 asymptomatic renal transplant candidates prior to inclusion on the renal transplant waiting list. Based on clinical risk factors, 349 patients (74.9%) were defined as high-risk patients. In 227 of these patients (64.9%), non-invasive cardiac stress testing was performed [203 patients (89.4%) underwent myocardial scintigraphy and 24 patients (10.6%) underwent dobutamin stress echocardiography]. In 122 high-risk patients (35.1%), no non-invasive cardiac stress test was performed. In 25 of these patients (20.5%), screening was not finished at 19 May 2008 (end of the study). In 11 patients (9.0%), a coronary angiography was performed without prior non-invasive cardiac stress testing and 13 patients (10.7%) were excluded from transplantation due to non-cardiac reasons. In the remaining 73 high-risk patients (59.8%), the nephrologist decided not to do a non-invasive cardiac stress test, although the patients belonged to the high-risk group. These patients had significantly less cardiovascular risk factors compared to the high-risk patients with cardiac stress testing (Table 1). In 46 of the 73 patients (63%), age and/or smoking were the only clinical risk factor.

Results of non-invasive cardiac stress tests. In 15 of the 227 (6.6%), non-invasive cardiac stress tests, significant ischaemia was found (reversible defect in two or more segments). All 15 patients with significant ischaemia on non-invasive cardiac stress testing were male. No
other significant baseline differences were found between patients with cardiac ischaemia versus without ischaemia.

The incidence of significant cardiac ischaemia in patients with the highest risk [diabetes or a history of cardiovascular disease (n = 117)] was 8.5%. In 48 of the patients (21.1%), one or more fixed defects were found.

**Coronary angiography and revascularization.** In 10 of the 15 patients with significant cardiac ischaemia, a coronary angiography was performed. In eight patients, significant coronary artery disease in one or more vessels was found (none of the patients had three vessel disease). In Figure 1, a flow diagram of the cardiac evaluation process is given.

In five patients with significant coronary artery disease, a PCI was performed before wait-listing (none underwent CAG). No complications were observed in these patients.

In 19 patients with fixed defects in one or more segments, a coronary angiography was performed. Ten of these patients had significant coronary artery disease and four patients underwent revascularization before wait-listing (three PCI and one CAG).

**Acceptance for the waiting list.** Of the 349 high-risk renal transplant candidates, 275 patients (78.8%) were accepted for the waiting list for renal transplantation [195 of the 227 patients (85.9%) who underwent non-invasive cardiac stress testing and 80 of the 122 patients (65.6%) without stress testing]. Twelve patients (3.4%) were excluded due to a cardiac cause.

The median time between the start of the evaluation and the decision about wait-listing was 5 (1–44) months. The mean time between non-invasive cardiac testing and renal transplantation was 14 ± 11 months.

Renal transplantation. In total, 160 of the 349 high-risk patients received a renal transplantation (screening group) (Figure 1). The baseline characteristics are given in Table 2. Non-invasive cardiac stress testing was performed in 110 patients. Six patients underwent preoperative revascularization. Four of the 15 patients with significant ischaemia on non-invasive cardiac stress testing received a renal transplantation (all had significant coronary artery disease and three patients were treated with PCI before transplantation). The other three patients that underwent preoperative revascularization (two PCI and one CAG) had one or more fixed defects on non-invasive cardiac stress testing (data about cardiac evaluation and revascularization are given in Table 3).

**Perioperative cardiac events after transplantation.** In the first 30 days after transplantation, six perioperative cardiac events (3.8%) were observed (all non-STEMI). All events occurred in patients with negative non-invasive cardiac stress testing (none of these patients underwent CAG or revascularization).

**Historical control group.** Between 2000 and 2004, we evaluated 375 asymptomatic renal transplant candidates in our outpatient clinic. Based on clinical risk factors, 298 were retrospectively defined as high-risk patients. In 95 patients (31.9%), non-invasive cardiac stress testing was performed (six patients had significant cardiac ischaemia). The clinical consequences of non-invasive cardiac stress testing were low (only one patient with ischaemia was excluded from transplantation and only one patient underwent preoperative revascularization). Two hundred and thirty-two high-risk patients (77.8%) were accepted for the waiting list [10 patients (3.4%) were rejected due to a cardiac cause]. There was no significant difference in the percentage of patients that were accepted for the waiting list before and after the introduction of the standard cardiac workup. The time between the start of the evaluation and the decision about wait-listing was significantly longer in the control group [6 (1–66) months in the control group versus 5 (1–44) in the study group (P < 0.01)]. There was no significant difference in the time between wait-listing and transplantation between both groups. One hundred and seventy-two of the 298 high-risk patients (57.7%) received a renal transplantation.

**Comparison with historical control group.** In Table 2, the baseline characteristics of the screening and control group are given. Significantly more patients in the screening group received a pre-emptive transplantation, received a kidney from a living donor and received a previous renal transplantation, and significantly more patients in the screening group were treated with a beta-blocker. There were no significant differences in cardiovascular risk factors between the screening and the control group. Six patients in the screening group versus two in the control group underwent preoperative revascularization (Table 3).

Cardiac events in study and historical control groups. The incidence of perioperative cardiac events
was 6 (3.8%) in the screening group compared to 13 (7.6%) in the historical control group \( (P = 0.136) \). Although there was no significant difference in the total number of events, the severity of the events differed: three cardiac deaths, five STEMI and five non-STEMI \( \text{[three patients had a peak troponin >3 lg/L (range 5.2–10.40 lg/L)]} \) in the control group compared to six non-STEMI \( \text{[one patient had a peak troponin >3 lg/L (54.10 lg/L)]} \) in the screening group.

Significantly, more major perioperative cardiac events occurred in the control group compared to the screening group \( (11 \text{ major events in the control group versus 1 major event in the screening group, } P < 0.05) \).

Patients with a perioperative cardiac event had significantly more cardiac risk factors compared to patients without a perioperative cardiac event \( \text{[respectively, 73.7 versus 49.2% had two or more cardiac risk factors (} P < 0.05) \text{]} \). The number of events was too small to perform a multivariate analysis.

**Discussion**

In 2004, we introduced a standardized cardiac risk assessment programme for asymptomatic high-risk renal transplant candidates in our centre. Based on our retrospective analysis, two important conclusions can be drawn. Firstly, the incidence of significant cardiac ischaemia in asymptomatic high-risk renal transplant candidates was low and as a consequence, only a few patients underwent preoperative revascularization. Secondly, there was no significant decrease in the overall incidence of perioperative

**Table 2.** Baseline characteristics of all asymptomatic high-risk renal transplant candidates that received a renal transplantation (screening and historical control group)

<table>
<thead>
<tr>
<th></th>
<th>Screening group ( (n = 160) )</th>
<th>Control group ( (n = 172) )</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient age (year)</td>
<td>50.8 ± 12.1</td>
<td>51.1 ± 12.1</td>
<td>0.83</td>
</tr>
<tr>
<td>Male (%)</td>
<td>106 (66.2)</td>
<td>109 (63.4)</td>
<td>0.58</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25.2 ± 3.9</td>
<td>25.4 ± 4.4</td>
<td>0.06</td>
</tr>
<tr>
<td>Dialysis (%)</td>
<td>124 (77.5)</td>
<td>160 (93.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetic nephropathy (%)</td>
<td>14 (8.8)</td>
<td>19 (11.0)</td>
<td>0.58</td>
</tr>
<tr>
<td>Previous renal transplantation (%)</td>
<td>19 (11.9)</td>
<td>11 (6.4)</td>
<td>&lt;0.08</td>
</tr>
<tr>
<td>Living donor (%)</td>
<td>94 (58.8)</td>
<td>61 (35.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiovascular risk factor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>20 (12.5)</td>
<td>27 (15.5)</td>
<td>0.51</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>47 (29.4)</td>
<td>50 (15.7)</td>
<td>0.95</td>
</tr>
<tr>
<td>ACS (%)</td>
<td>9 (5.6)</td>
<td>12 (7.5)</td>
<td>0.61</td>
</tr>
<tr>
<td>PCI/CAG (%)</td>
<td>9 (5.6)</td>
<td>6 (3.5)</td>
<td>0.52</td>
</tr>
<tr>
<td>Peripheral vessel disease (%)</td>
<td>14 (8.8)</td>
<td>20 (11.6)</td>
<td>0.39</td>
</tr>
<tr>
<td>TIA/stroke (%)</td>
<td>21 (13.1)</td>
<td>13 (7.6)</td>
<td>0.27</td>
</tr>
<tr>
<td>Current smoking (%)</td>
<td>59 (36.9)</td>
<td>56 (32.6)</td>
<td>0.24</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;45 years (male) (%)</td>
<td>769 (49.4)</td>
<td>94 (54.7)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>&gt;55 years (female) (%)</td>
<td>26 (16.2)</td>
<td>23 (13.4)</td>
<td>0.20</td>
</tr>
<tr>
<td>Obesity (%)</td>
<td>21 (13.1)</td>
<td>27 (15.7)</td>
<td>0.50</td>
</tr>
<tr>
<td>Abnormal ECG (%)</td>
<td>25 (15.6)</td>
<td>28 (16.3)</td>
<td>0.87</td>
</tr>
<tr>
<td>Number of cardiovascular risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 risk factor (%)</td>
<td>80 (50.0)</td>
<td>84 (48.8)</td>
<td>0.83</td>
</tr>
<tr>
<td>2 risk factor (%)</td>
<td>50 (31.2)</td>
<td>55 (32.0)</td>
<td>0.89</td>
</tr>
<tr>
<td>3 risk factors (%)</td>
<td>22 (13.8)</td>
<td>23 (13.4)</td>
<td>0.48</td>
</tr>
<tr>
<td>≥4 risk factors (%)</td>
<td>8 (5.0)</td>
<td>10 (5.9)</td>
<td>0.47</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta-blocker (%)</td>
<td>143 (89.4)</td>
<td>130 (75.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Aspirin (%)</td>
<td>37 (23.1)</td>
<td>28 (16.3)</td>
<td>0.34</td>
</tr>
<tr>
<td>Statin (%)</td>
<td>77 (48.1)</td>
<td>64 (37.2)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

**Fig. 1.** Cardiac evaluation and perioperative cardiac events in renal transplant candidates evaluated > 1 January 2004.
cardiac events after the introduction of the standardized protocol.

**Incidence of significant cardiac ischaemia**

The incidence of cardiac ischaemia in our study was lower compared to previous studies. In previous studies, the incidence of cardiac ischaemia was between 14 and 40% [11, 18, 21]. In most of these studies, non-invasive cardiac stress tests with reversible defects in only one segment were defined as positive. In our study, as also in daily clinical practice, only non-invasive cardiac stress tests with reversible defects in at least two or more segments were defined as positive. In the meta-analysis of Etchells et al. [22], there was no increased risk of perioperative cardiac events if reversible ischaemia is present in <20% of the left ventricle.

In our study population, the incidence of diabetes mellitus was lower compared to other studies [17, 23]. This is caused by the lower incidence of diabetes in the Netherlands compared to the United States. The relatively low risk of our study population could be the reason for the low incidence of significant cardiac ischaemia. The low incidence of significant cardiac ischaemia in patients with the highest risk (patients with diabetes and a history of cardiovascular disease) argues against this theory.

Furthermore, the low incidence of significant ischaemia might reflect a decrease in significant coronary artery disease due to an increase in pre-emptive transplantations and improved treatment of cardiovascular risk factors after 2004.

In the literature, there is no consensus about the true value of non-invasive cardiac stress testing in ESRD. In some studies, a low sensitivity of non-invasive cardiac evaluation is found but other studies found a high sensitivity and high negative predictive value [9, 17, 18, 24]. In our study, six patients with a negative non-invasive cardiac stress test had a perioperative cardiac event. We cannot exclude that the low incidence of positive non-invasive cardiac stress testing in our study is related to a low sensitivity of the test in patients with ESRD. Although there is doubt about the value of non-invasive cardiac stress testing in ESRD patients, Patel et al. [17] showed that exercise tolerance testing can give important prognostic information.

**Coronary interventions**

As a consequence of the low incidence of cardiac ischaemia, the incidence of preoperative revascularization in our study was low. Despite the fact that the number of non-invasive cardiac stress test doubled after the introduction of our standardized screening programme, there was no significant increase in the number of preoperative revascularizations. Several other studies also found a low incidence of revascularization after pre-transplant cardiac stress testing [17, 25, 26]. Due to this finding, we cannot make a statement that pre-transplant revascularization is beneficial. In observational studies, no benefit of pre-transplant revascularization was found [17, 27]. Unfortunately, no large randomized controlled clinical trials (RCT) have been performed in renal transplant candidates [27]. Yet, in two RCTs, no benefit of preoperative revascularization was found in patients undergoing major vascular surgery [14, 28].

**Perioperative cardiac events**

In accordance with the low incidence of cardiac ischaemia, no significant decrease in the incidence of perioperative cardiac events was observed after the introduction of our standardized cardiac risk assessment protocol. However, there was a trend to a decrease in perioperative cardiac events and significantly less major perioperative cardiac events were observed after the introduction of the screening programme. First, we cannot exclude that these differences are related to the implementation of the screening programme. Secondly, this finding could also be due to improved perioperative medical treatment. Significantly, more patients were treated with beta-blockers. Most studies in patients undergoing major non-cardiac surgery found a decrease in perioperative cardiac events in patients treated with beta-blockers [29]. Furthermore, an increased number of patients were treated with aspirin and statins. During the last few years, we continued aspirin perioperatively. First, we discontinued aspirin a few days before transplantation to minimize bleeding complications and to do a renal biopsy postoperatively when indicated. Both the use of statins and aspirin are associated with less perioperative cardiac events [30–32]. Thirdly, in 11 of the 15 patients with significant cardiac ischaemia, no renal transplantation was performed yet due to the long waiting time of 4–5 years in The Netherlands. Earlier studies showed that patients with significant cardiac ischaemia on non-invasive cardiac stress testing have an increased risk for perioperative myocardial infarction [24]. On the contrary, there is no evidence that revascularization is better than best medical treatment alone in reducing the perioperative risk in patients with inducible ischaemia [14, 15, 17]. Although, non-invasive cardiac stress testing might be helpful in identifying high-risk patients, there is no evidence of improved clinical outcome after revascularization compared to best medical treatment. Finally, the decrease we found in

### Table 3. Cardiac evaluation and outcome in the screening and historical control group

<table>
<thead>
<tr>
<th></th>
<th>Screening group</th>
<th>Control group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 160)</td>
<td>(n = 172)</td>
<td></td>
</tr>
<tr>
<td>Non-invasive stress test (%)</td>
<td>110 (68.8)</td>
<td>53 (30.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Significant ischaemia (%)</td>
<td>4 (3.6)</td>
<td>3 (5.7)</td>
<td>0.68</td>
</tr>
<tr>
<td>Coronary angiography (%)</td>
<td>20 (12.5)</td>
<td>13 (7.6)</td>
<td>0.13</td>
</tr>
<tr>
<td>Significant coronary artery disease (%)</td>
<td>11 (55)</td>
<td>4 (30.7)</td>
<td>0.13</td>
</tr>
<tr>
<td>Revascularization (%)</td>
<td>6 (3.8)</td>
<td>2 (1.2)</td>
<td>0.27</td>
</tr>
<tr>
<td>PCI (%)</td>
<td>5 (83.3)</td>
<td>2 (100)</td>
<td></td>
</tr>
<tr>
<td>CAG (%)</td>
<td>1 (16.7)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Cardiac event &lt; 30 days (%)</td>
<td>6 (3.8)</td>
<td>13 (7.5)</td>
<td>0.136</td>
</tr>
<tr>
<td>Non-STEMI (%)</td>
<td>6 (100)</td>
<td>5 (38.4)</td>
<td>0.76</td>
</tr>
<tr>
<td>STEMI (%)</td>
<td>0</td>
<td>5 (38.4)</td>
<td>0.061</td>
</tr>
<tr>
<td>Cardiac death (%)</td>
<td>0</td>
<td>3 (23.1)</td>
<td>0.25</td>
</tr>
</tbody>
</table>
major cardiac events could be explained by differences in baseline characteristics between the two groups before and after standardized cardiac risk assessment. More patients in the screening group received a pre-emptive transplantation and therefore were not exposed to the harmful effects of dialysis. However, no differences in cardiovascular risk factors were found.

Limitations of the study

Our study has several limitations: (i) our study is limited by its retrospective design; (ii) the protocol was violated by the treating physician in 20% of the high-risk patients and no non-invasive cardiac stress tests were performed. The reason for non-adherence might be our broad definition of high risk. Patients without cardiac stress testing had significantly less risk factors (>50% had only smoking or increased age as risk factor). It is likely that clinicians did not perform cardiac stress tests in young patients in good clinical condition with only one risk factor. In these patients, no perioperative cardiac events were observed. Furthermore, violation of the protocol could be due to the growing evidence during the study that preoperative revascularization is not superior to optimal medical treatment [14, 15]; (iii) comparison with a historical control group can be criticized. Firstly, there was a difference in the treatment of cardiac risk factors between the study and control group. Secondly, 32% of the high-risk patients in the control group underwent non-invasive cardiac stress testing and some underwent revascularization. Despite its limitations, comparison with a historical control group gives valuable information about the effect of introducing a standard cardiac evaluation programme; (iv) we did not collect data about cardiac events in the time between evaluation and transplantation. Data about the occurrence of cardiac events in this time period could have given more information about the value of non-invasive cardiac stress testing; (v) we did not have complete information about the left ventricle ejection fraction in our study. Previous studies showed that the left ventricle ejection fraction is a strong prognostic marker for cardiac events in ESRD patients awaiting renal transplantation [10]; (vi) the mean delay between non-invasive cardiac stress testing and transplantation was 14 months. It is possible that a stress test closer to the transplantation might have a better prognostic value. Despite its limitations, information from observational studies like ours is necessary as long as no randomized controlled clinical trials compared preoperative revascularization to optimal medical treatment alone in renal transplant candidates. Unfortunately, it is not very likely that such a randomized controlled clinical trial will be set up in renal transplant candidates [17].

In conclusion, non-invasive cardiac stress testing in high-risk renal transplant candidates had little clinical consequences and no significant decrease in perioperative cardiac events was observed after the introduction of a standard cardiac evaluation programme. Our study suggests that non-invasive cardiac stress testing in all high-risk renal transplant candidates is unnecessary. Because of the small sample size, the relatively low-risk profile of our study group and the significant difference in major perioperative cardiac events between the screening and control group, a final conclusion about the necessity of non-invasive cardiac stress testing in all high-risk renal transplant candidates, cannot be drawn solely on our study. Prospective, randomized studies will be necessary to draw a final conclusion about the effect of non-invasive cardiac evaluation and intervention in high-risk renal transplant candidates.

Based on our results and the fact that there is no evidence that preoperative revascularization is better than medical treatment alone, we believe that non-invasive cardiac stress testing in all high-risk renal transplant candidates should not be recommended. Revascularization should be restricted to those patients with an indication for revascularization regardless of the transplantation. Although the guidelines for preoperative cardiac risk assessment and perioperative cardiac management of the European Society of Cardiology are not directly applicable to chronic renal failure patients, we propose to follow these guidelines in renal transplant candidates as long as evidence from randomized clinical trials in renal transplant recipients is lacking [33]. These guidelines recommend restricting non-invasive cardiac stress testing to patients with a low functional capacity (inability to climb two flights of stairs) and three or more cardiovascular risk factors undergoing high-risk surgery. All other patients should only receive maximal medical treatment (low-dose titrated beta-blocker, statins and an angiotensin converting enzyme inhibitor in case of systolic left ventricle dysfunction). Thus, non-invasive cardiac stress testing in all high-risk asymptomatic renal transplant candidates did not significantly decrease the incidence of perioperative cardiac events and is therefore not recommended.

Conflict of interest statement. None declared.

References


33. Poldermans D, Bax JJ, Boersma E et al. Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery: The Task Force for Preoperative Cardiac Risk Assessment and Perioperative Cardiac Management in Non-cardiac Surgery of the European Society of Cardiology (ESC) and endorsed by the European Society of Anaesthesiology (ESA). *Eur Heart J* 2009; 30: 2769–2812

Received for publication: 20.4.10; Accepted in revised form: 17.12.10