NICE National Institute for Health and Care Excellence

2023 exceptional surveillance of renal replacement therapy and conservative management (NICE guideline NG107)

Surveillance report

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Surveillance decision

We will not update the NICE guideline on renal replacement therapy and conservative management in relation to cardiac assessment before transplantation.

Reasons for the decision

The guideline does not currently include recommendations about cardiac assessment before transplantation because there was no evidence on this subject at the time it was developed. This review considered new evidence related to the following recommendation for research: What is the clinical and cost effectiveness of cardiac assessment before transplantation?

We identified 3 observational studies which were relevant to this question but this was deemed insufficient evidence to support an update of the guideline to clarify whether cardiac assessment should be used before transplantation.

Exceptional surveillance review summary

Reason for the exceptional review

NICE was contacted by NHS England and asked to check if the evidence base of cardiac assessment before kidney transplantation had developed sufficiently to support an update of the NICE guideline on renal replacement therapy and conservative management.

This follows publication of the Renal Medicine Getting It Right First Time (GIRFT) report from March 2021, which includes a recommendation to 'approach NICE to develop a national guideline for suitability for transplant listing to be developed which is patient-centred and adopted in a consistent manner across all networks'.

Background

During development of the NICE guideline, the committee made the following observations:

- Despite pre-kidney-transplant screening investigations with cardiac assessment being common care to minimise perioperative risk, the evidence base and utility of such assessment is not well established.
- There may be benefits of cardiac assessment in preparation for transplant in terms of preventing people with excessively high cardiovascular risk from being inappropriately exposed to the risks of surgery, allowing people to optimise their cardiovascular risk profile before surgery and promoting the most effective use of potential kidney transplants. However, there are considerable harms involved as cardiac assessment can delay the patient pathway towards transplantation and there are also potential harms associated with each individual cardiac assessment. Given the magnitude and uncertainty of these benefits and harms, as well as the current variability of service provision, this was considered an important area for a recommendation for research.

The guideline committee made a recommendation for research to inform future practice as there was no evidence that met the review protocol on cardiac assessment before transplantation.

Methods

The exceptional surveillance process consisted of:

- Literature searches to identify relevant evidence.
- Examining the NICE event tracker for relevant ongoing and published events.
- A search for ongoing research.
- Assessing the new evidence to determine whether or not to update sections of the guideline.

For further details about the process and the possible update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Search and selection strategy

We searched for new evidence related to cardiac assessment before transplantation, which relates to the section on preparing for renal replacement therapy or conservative management and the recommendation for research on cardiac assessment.

Selecting relevant studies

The recommendation for research on cardiac assessment sought to answer the following question: What is the clinical and cost effectiveness of cardiac assessment before transplantation?

Due to the scope of the existing review protocol (which included people considering renal replacement therapy) and the lack of existing evidence, we opted to include studies that either 1) included people before cardiac assessment and transplant listing, or 2) included people who had already undergone initial assessment and were identified as suitable candidates for transplant or were waitlisted for transplant and undergoing follow-up assessments. We also included studies where the patient population had non-invasive or invasive tests for cardiac assessment and was compared with patient populations where no screening test was used. Randomised controlled trials (RCTs) were prioritised, but non-randomised studies were considered where outcomes were adjusted for key confounders, such as age, health at baseline and comorbidities.

We found 3 studies in a search for RCTs, non-randomised studies and systematic reviews published between 1 December 2017 and 21 March 2023. One was a prospective and 2 were retrospective cohort studies.

No new evidence was available for cardiac assessment in children and young people. This remains an evidence gap.

Summary findings from included studies

UK study of up to 5-year post-transplant outcomes for transplant candidates with or without screening

A national prospective cohort study in England (Nimmo et al. 2020) investigated whether transplant candidate screening with a stress test or invasive coronary angiogram for asymptomatic coronary artery disease was associated with any difference in major adverse cardiac events (MACE) up to 5 years post-transplantation. Overall, 2,572 individuals were transplanted in 18 centres between 2011 to 2017. The incidence of MACE post-transplant at 90 days, 1 and 5 years was 0.9%, 2.1% and 9.4% respectively. Prior to propensity-score matching, patients undergoing screening had a higher incidence of MACE at 1 and 5 years (18 screening versus 34 no screening patients had an event at 1 year; 66 screening versus 133 no screening patients had an event at 5 years). No

difference was observed at 90 days post-transplant.

After propensity-score matching based on age, sex, ethnicity, socioeconomic status, smoking history, history of diabetes, ischemic heart disease, peripheral vascular disease, and cerebrovascular disease, 1,760 individuals were examined (880 each in the screened and unscreened groups). There was no statistically significant association between screening and MACE at 90 days (hazard ratio [HR] 0.80, 95% confidence interval [CI] 0.31 to 2.05), 1 year (HR 1.12, 95% CI 0.51 to 2.47) or 5 years (HR 1.31, 95% CI 0.86 to 1.99). There was no association between screening for asymptomatic coronary artery disease and MACE up to 5 years post-transplant. An important limitation of this study is that it provides no information about individuals who had cardiac assessment but were then excluded from the transplant pathway.

US study #1 of 30-day post-transplant outcomes for transplant candidates with or without screening.

A national retrospective cohort study in the United States (Cheng et al. 2023) investigated whether invasive or non-invasive testing for coronary heart disease in asymptomatic kidney transplant candidates in the year of the kidney transplant is associated with reduced early post-transplant death or myocardial infarction (MI). An instrumental variable (IV) analysis was used, with the programme-level coronary heart disease (CHD) testing rate in the year of the transplant as the IV. Analyses were stratified by study period, as the rate of CHD testing varied over time. The primary outcome was a composite of death or acute MI within 30 days of after kidney transplant.

Using data from the US Renal Data System and Medicare claims from 2000 to 2014, the cohort comprised 79,334 adult, first-time kidney transplant recipients. The primary outcome occurred in 4,604 patients (5.3%; 2,063 [2.6%] death, 2,329 [2.9%] acute MI). In the main IV analysis, compared with no testing, CHD testing was not associated with a change in the rate of primary outcome (rate difference, 1.9%; 95% CI, 0% to 3.5%). The results were similar across study periods, except for 2000 to 2003, during which CHD testing was associated with a higher event rate (rate difference, 6.8%; 95% CI, 1.8% to 12.0%).

US study #2 of 30-day post-transplant outcomes for transplant candidates with or without screening.

A national retrospective cohort study in the United States (Dunn et al. 2019) sought to

establish if cardiac stress testing after placement on the waitlist, prior to kidney transplantation would not reduce postoperative death, total MI or fatal MI. Data were extracted from the United States Renal Data System for end stage renal disease patients; they were over 40 years old with primary Medicare insurance and received their first kidney transplant between 2006 and 2013; patients who received coronary angiography without stress testing in the 18 months prior to transplant were excluded. Propensity matching created a 1:1 matched sample of patients with and without stress testing in the 18 months prior to kidney transplantation. Propensity matching eliminated differences in demographics, identified risk factors and comorbidities between groups.

In the propensity-matched cohort of 17,304 patients, death within 30 days occurred in 72 of 8,652 (0.83%) patients who underwent stress testing and in 65 of 8,652 (0.75%) patients who did not (odds ratio [OR] 1.07; 95% CI: 0.79 to 1.45; p=0.66). MI within 30 days occurred in 339 (3.9%) patients who had a stress test and in 333 (3.8%) patients who did not (OR 1.03; 95% CI: 0.89 to 1.21; p=0.68). Fatal MI occurred in 17 (0.20%) patients who underwent stress testing and 15 (0.17%) patients who did not (OR 0.97; 95% CI: 0.71 to 1.32; p=0.84).

Ongoing research

We checked for relevant ongoing research and one trial was assessed as relevant to the guideline recommendation for research:

- Screening for asymptomatic coronary artery disease in kidney transplant candidates (CARSK). This trial will test the hypothesis that eliminating screening tests for occult coronary artery disease after waitlisting is not inferior to regular screening for the prevention of MACE.

See ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual for more details on our consultation processes.

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

The available evidence from searches only identified 1 prospective and 2 retrospective cohort studies. Despite the limited evidence and differences across the studies and reported outcomes, there appears to be consistent findings regarding the utility of cardiac assessment: the 3 studies suggest that cardiac assessment for asymptomatic coronary artery disease after placement on the waitlist, prior to kidney transplantation, does not improve patient outcomes.

There are however some uncertainties stemming from these studies. Given they employed observed transplant outcomes, the patients were already assessed as suitable candidates for placement on the transplant waiting list and may have had prior, unspecified assessments before placement on the waiting list; the subgroups may have also had prior assessments outside the study period of interest of the respective studies. Furthermore, while the included participants may be lower risk patients, there may be different risk-stratification or assessment approaches applied in different settings prior to waitlisting. Overall, there is uncertainty in the transplant candidate sub-populations that the findings would apply to. Furthermore, we cannot know how many patients were never listed for transplant due to prior detection of existing health problems.

The accuracy and completeness of key study variables in the data sources employed by the individual papers are also unknown. These are not reported in the available information in the retrospective studies, and it is unknown if the diagnoses were accurately recorded. In addition, the extent of linkage errors or mismatches between the utilised data sources raises potential to produce biased analysis.

From these studies, there was also limited information about the exact timing, frequency or type of screening investigations, and it was likely to be highly variable across national centres and internationally between the UK and US. There is also no information about the reasons for not employing pre-transplant assessments in the no screening cases.

No randomised trials were identified from our searches. We have, however, identified the ongoing CARSK randomised trial (n=3,306 participants). However, the applicability of the study to English settings is uncertain as it is looking at regular use of non-invasive screening tests, after screening for wait list entry. We will continue to monitor this study and consider the findings when they become available.

Given the evidence is limited to 3 observational studies that have different populations of

interest and the uncertainties associated with the poor-quality evidence, it would seem prudent to wait for more confirmatory evidence regarding the effectiveness of cardiac assessment in pre-transplant evaluation that addresses the NICE recommendation for research on cardiac assessment.

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