International Journal of Cardiology 191 (2015) 7–10

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Letter to the Editor

Chronic alcoholic donors in heart transplantation: A mortality meta-analysis

Kirolos A. Jacob *, Linda M. de Heer, Frederiek de Heer, Jolanda Kluin

Department of Cardiothoracic Surgery, University Medical Centre Utrecht, Utrecht, The Netherlands

ARTICLE INFO

Article history:
Received 9 April 2015
Accepted 30 April 2015
Available online 1 May 2015

Keywords:
Cardiac transplantation
Alcoholic donor
Mortality
Rejection
Graft dysfunction

Heart transplantation is presently one of the few accepted long-term treatments for end-stage heart failure not responsive to maximal medical management [1]. The number of heart failure patients has risen dramatically in recent years, while the number of heart donors has remained stable, resulting in a growing supply/demand mismatch. This supply/demand disparity results into substantial mortality (20%–50%) for patients awaiting cardiac transplantation [2]. Bridging devices are expensive and can increase the costs of an already costly operation. The need for less strict criteria of the donor pool has been opted by several experts [1,2], necessitating re-evaluation of criteria for a marginal donor organ which are currently being repealed. Based on outdated literature [3,4], the International Guidelines advise against transplantation of hearts from alcoholic donors, present in 10–20% of cases [4–6], as alcohol could be toxic to myocytes. This review aimed to analyze the mortality rates at follow-up in patients receiving hearts from alcoholic donors.

A systematic search of Medline, Embase, CINAHL and Cochrane Library was performed reviewing articles published up to February 2014. A search filter was designed using synonyms for domain, i.e. patients undergoing heart transplantation, determinant, i.e. alcoholic donor hearts versus non-alcoholic donor hearts, and outcome, i.e. mortality and/or rejection at follow-up. Articles were selected based on predetermined inclusion criteria, being: observational cohort studies reporting on adult human subjects who underwent a heart transplantation from an alcoholic donor. Primary outcome was classified as mortality rates at follow-up more than 12 months in the alcoholic donor group (ADG) versus the non-alcoholic donor group (NADG). Graft rejection or severe graft dysfunction, at ≥1 months of follow-up, was considered a secondary outcome. All included studies were assessed for quality according to the Newcastle-Ottawa Quality Assessment Scale (NOS) for cohort studies [7]. Data analysis was performed using the random-effects mode with Review Manager Software (Review Manager (RevMan) version 5.3, the Cochrane Collaboration, 2014). Relative risk (RR) and 95% confidence intervals (CIs) were calculated for each independent study and for the summary statistic, with values of <1 favoring the ADG. This means that if the risk difference is under the number 1, the mortality rates are higher in the ADG. χ^2 tests were used to study heterogeneity between studies [8]. Publication bias was estimated with the weighted regression test of Egger.

Overall 485 articles were identified and six articles were included in this meta-analysis (Fig. 1). All but two articles [4,9] achieved maximum score of the NOS (Table 1).

Mean incidence of alcoholism in heart donors was 15.8%. Follow-up in the studies ranged from 24 to over 43 months. Baseline and surgical characteristics in the donor population and in the recipient population were stated by four studies [3,5,6,10] and were similar in the ADG and NADG groups (Table 2). Mortality rates were stated by four studies [3,6,9,10]. Pooled mortality was 23.2% (range 7.1% to 48.4%) in the ADG and 20.3% (range 8.5% to 43.8%) in the NADG, in a follow-up period of 2–4 years after transplantation. Pooled relative risk for mortality was found to be insignificant (RR: 1.19 (95% CI: 0.57 to 2.48)) (Fig. 2A) [3,6,9,10]. Rejection/graft dysfunction rates at 1 to 43 months of follow-up were stated by four studies [3–5,10]. Overall pooled risk of graft rejection was 27.0% (range 5.1% to 50%) in the ADG and 20.3% (range 5.2% to 39%) in the NADG. An insignificant relative risk was calculated, i.e. 1.40 (95% CI: 0.77 to 2.53) (Fig. 2B) [3–5,10]. Statistical heterogeneity was evident among the studies reporting mortality rates ($\chi^2 = 17.7$, $P = 0.0007$), and graft rejection rates ($\chi^2 = 9.22$, $P = 0.03$). We recorded no evidence of publication bias by the Egger test ($P < 0.05$).

To our knowledge this is the first meta-analysis on the effects of receiving an alcoholic donor's heart and survival. In contrast to the two articles that form the basis of the current guidelines [3,4,11], this meta-analysis shows that hearts from alcoholic donors do not result in higher mortality and graft rejection rates in recipients when compared to hearts from non-alcoholic donors. Since alcohol abuse in donors is prevalent in 10–20% potential donors, inclusion of hearts from alcoholic

* Corresponding author at: University Medical Center Utrecht, Department of Cardiothoracic Surgery, Mail Stop E03.511, PO Box 85500, 3508 GA Utrecht, The Netherlands.
E-mail address: k.a.jacob@umcutrecht.nl (K.A. Jacob).

http://dx.doi.org/10.1016/j.ijcard.2015.04.253
0167-5273/

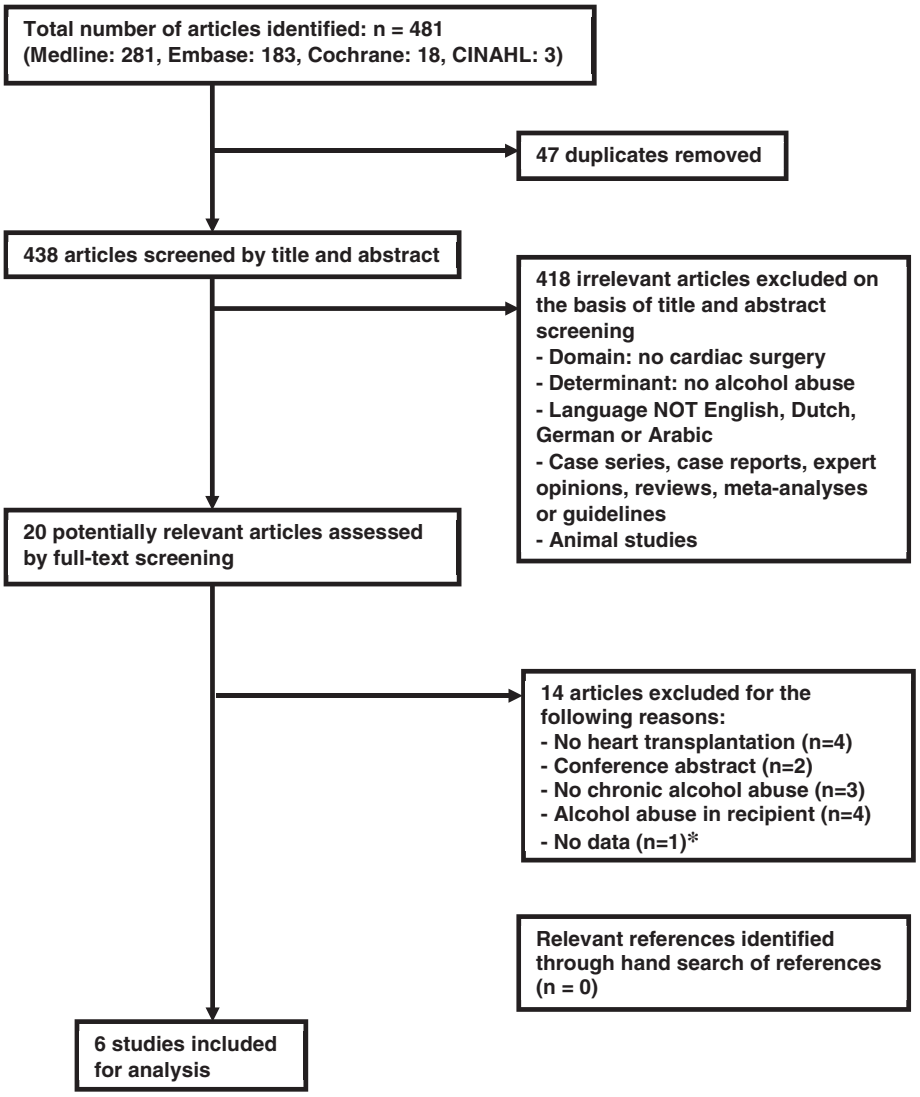

Fig. 1. Study selection process. CINAHL: cumulative index to nursing and allied health. *: No data found in the study by Tsao et al. [12].

donors would result in a larger donor pool. Based on our findings we think and would like to highlight the fact that exclusion of a potential heart donor solely based on his/her alcohol abuse should not be advocated anymore. However one still has to be cautious: chronic alcohol abuse can result in alcoholic cardiomyopathy in the donor, warranting careful pre-transplantation echocardiography. Certainly, these alcoholic donor hearts should not be used for transplantation. Thus, cardiac surgeons and cardiologists should not rely solely on alcohol abuse in donors as not being a risk factor for the aforestated poor outcomes, but also take other risk factors into account.

One of the main limitations of this meta-analysis is selection bias. No detailed information about the allocation algorism or the recipient selection for these grafts was at hand, and demographic and clinical differences between the ADG and NADG groups could act as confounding factors. Nevertheless, donor as well as recipient baseline, surgical and intra-operative variables were investigated by four studies and were

Table 1
Quality assessment of included studies. *: A study can be awarded a maximum of 1 star for each numbered item in the selection and outcome categories. A maximum of two stars can be given for comparability. #: In this case of mortality studies, outcome of interest is presence of an incident or complication or rejection event, rather than death. §: Before assessing the quality of all studies, a follow-up duration of over 12 months was decided to be sufficient for the primary outcome, i.e. mortality, and a duration of 1 month for the secondary outcome, i.e. severe graft rejection. NA: not applicable.

Author, year	Selection				Comparability of cohorts	Outcome		
	Representativeness of exposed cohort	Representativeness of non-exposed cohort	Ascertainment of exposure	Outcome not present at beginning of study, #		Assessment of outcome	Was follow-up long enough	Adequacy of follow-up, §
Fiorelli et al., 2012	*	*	*	NA	**	*	*	*
Bonde et al., 2010	*	*	*	NA	*	*	*	*
Shea et al., 2007	*	–	*	NA	–	*	*	–
De La Zerda, 2007	*	*	*	*	**	*	*	*
Freimark et al., 1996	*	*	*	NA	**	*	*	*
Houyel et al., 1992	*	–	*	NA	–	*	*	*