

Impact of early central venous catheter removal on outcome in patients with candidaemia

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ABSTRACT

Removal of central venous catheters (CVCs) from candidaemic patients is considered the reference standard of care, although this practice is not always possible. The impact of prompt catheter removal on outcome was investigated by analysing data from an active population-based surveillance study in Barcelona, Spain. Patients with candidaemia and a CVC were identified between January 2002 and December 2003. Cases with CVC removal within 2 days were classified as having early CVC removal. Outcome, defined as in-hospital mortality 2–30 days after diagnosis of candidaemia, was determined among hospitalised adults using univariate, Kaplan–Meier and multivariate logistic regression analysis. Outpatients, paediatric patients and those who died or were discharged within 2 days were excluded. The study identified 265 patients with candidaemia and a CVC. Median time from diagnosis of candidaemia to catheter removal was 1 day (range 0–29 days). Overall, 172 patients met the criteria for inclusion in the outcome study. Patients with early CVC removal differed significantly from those with delayed CVC removal. According to univariate, Kaplan–Meier and multivariate analysis, the marker most predictive of in-hospital mortality among candidaemic patients with CVCs was severity of illness. These data suggest that timing of CVC removal may best be determined after carefully considering the risks and benefits to individual patients.

Keywords Candidaemia, central venous catheter, early removal, mortality, outcome, risk-factors

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INTRODUCTION

Several studies have identified central venous catheters (CVCs) as constituting an increased risk for the development of candidaemia [1–3]. Although removal of CVCs from candidaemic

patients is considered the reference standard of care [4,5], this practice is not always possible. Previous studies have investigated the impact of CVC removal on outcome, often defined as death, and the persistence or recurrence of candidaemia [1,4,6–14]. However, few data exist concerning the most appropriate time for CVC removal, or the sub-population of patients that would benefit most from such an intervention. A recent study, limited to patients suffering from cancer, attempted to answer these questions, and revealed an association between early CVC

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removal and improved outcome [14]. In order to provide a better description of a population with catheter-related candidaemia, and to understand the effect of early CVC removal on these patients, the present study analysed data from an active, population-based surveillance study of candidaemia [13].

PATIENTS AND METHODS

Study population and definitions

Prospective population-based surveillance for candidaemia was conducted in greater Barcelona (population 3.9 million) between 1 January 2002 and 31 December 2003 [13]. Fourteen major hospitals participated, ranging in size from 214 to 1295 beds. All candidaemic patients with a CVC in place for at least 24 h at the time of candidaemia were included in this analysis.

A candidaemia patient was defined as a resident of Barcelona for whom a *Candida* sp. was isolated from blood. Cases were defined as having primary candidaemia if there was no apparent portal of entry or if the infection was probably catheter-related. Secondary candidaemia cases were defined as patients with infections that occurred after a potential source of infection was identified. Catheter-related candidaemia was recorded when a patient had primary candidaemia and either (i) a catheter tip colonised with the same *Candida* sp. that was isolated from the bloodstream, or (ii) a quantitative blood culture sample obtained through the CVC that showed a \geq five-fold greater colony count than a concurrent peripheral venous quantitative blood culture. Significant colonisation of the catheter was defined by the isolation of >15 CFU of a *Candida* sp. using the roll-plate semiquantitative culture method [4,15].

Adult candidaemic patients with an APACHE II score ≥ 20 were defined as having a high severity of illness (SOI); adult candidaemic patients with an APACHE II score <20 were defined as having a low SOI.

To explore the effect of early catheter removal on outcome, patients with early CVC removal were defined as those who had the CVC removed on day 0 or 1 following the date of the incident candidaemia. Outcome was defined as in-hospital mortality measured at day 2–30 post-candidaemia onset. Patients who died or were discharged before day 2 post-candidaemia onset were excluded from the outcome analysis because it was not possible to classify these cases into either the early or delayed CVC removal categories. Inclusion of patients who died before a decision was made regarding removal could bias results towards showing an association between non-removal and death.

Outpatients, paediatric patients and patients with multiple CVCs were also excluded. Patients who developed candidaemia as outpatients would not have been subject to the outcome measure of in-hospital mortality. Paediatric patients were excluded because no SOI score was available. Patients with multiple CVCs were omitted because many did not have all CVCs removed on the same day, and therefore it was not possible to define the exact date of removal. Patients with multiple CVCs removed on the same day were also excluded, as inclusion of these patients was felt to bias the study population towards the group with CVCs removed.

Patients with early CVC removal were compared to those with delayed CVC removal by comparing the time to death for each of these groups using a Kaplan–Meier analysis. Kaplan–Meier curves were compared using the log-rank test. In addition, in-hospital mortality at 2–30 days post-candidaemia onset was examined by comparing early removal to delayed removal by univariate analysis. Stratified analysis was conducted among subgroups of patients in intensive care units (ICUs), those with preceding surgery, and those with malignancies. Statistical analysis was performed using SPSS software v.12.0 (SPSS Inc., Chicago, IL, USA) and SAS software v.8.2 (SAS Institute, Cary, NC, USA). Categorical variables were compared using chi-square analysis or Fisher's exact test, as appropriate. Median values were compared using the Wilcoxon rank sum test. Variables significant at $p < 0.2$ following univariate analysis, and other variables felt to confound the outcome, were included in a multivariate model that determined factors associated with in-hospital mortality at days 2–30 post-candidaemia.

Microbiological methods

Detection of candidaemia and identification of isolates to the species level were performed at the participating laboratories. Isolates were sent to the Mycology Reference Laboratory, National Center for Microbiology, Madrid, Spain for confirmation of species identity and antifungal susceptibility testing. Catheter tips were cultured by means of the semiquantitative roll-plate method described by Maki *et al.* [15].

RESULTS

Cases with CVCs

During the study period, 265 cases of candidaemia were detected in patients with CVCs. The majority of cases were episodes of primary candidaemia ($n = 251$, 95%); 145 (55%) of these had no apparent portal of entry, and 106 (45%) were probably catheter-related. Fourteen (5%) cases were classified as secondary candidaemia (Table 1).

At the time of candidaemia, 104 (40%) patients were admitted to an ICU, 80 (32%) were in medical wards, 50 (19%) were in surgical wards, and 13 (5%) were in paediatric wards; 11 (4%) were outpatients. Temporary non-tunnelled CVCs were the most common type of CVC (167 patients; 63%); 36 (14%) were peripherally inserted CVCs, 24 (9%) were infusion ports, and nine (3%) were tunnelled CVCs. In addition, 29 (11%) patients had multiple CVCs.

Candida albicans was isolated most frequently (48%), followed by *Candida parapsilosis* (26%), *Candida tropicalis* (10%), *Candida glabrata* (7%), *Candida krusei* (4%), and other *Candida* spp. (5%) (Table 1).

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