Congenital diaphragmatic hernia: a meta-analysis of mortality factors

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Authors' objectives
To critically review the importance of prenatal diagnosis, associated malformations, side of hernia, timing of surgery, and study population on mortality rates in patients with congenital diaphragmatic hernia (CDH).

Searching
MEDLINE, EMBASE and the Cochrane Library were searched from January 1975 to December 1998; the search terms were provided. The bibliographies of retrieved articles were checked for additional studies.

Study selection
Study designs of evaluations included in the review
Only full-length reports of studies published in English were included. Case reports, duplications, abstracts, and data on eventration were excluded. The studies had to report a detailed description of the study population, results on all CDH patients, and data on prenatal diagnosis and/or associated malformations.

Specific interventions included in the review
Only prenatal versus neonatal or later diagnoses will be reported in this abstract. The other interventions reported in the review included surgery at different time points.

Reference standard test against which the new test was compared
The review did not include any diagnostic accuracy studies that compared the performance of the index test with a reference standard of diagnosis.

Participants included in the review
The participants were foetuses and neonates with a pre- or postnatal diagnosis of CDH. The studies were categorised as foetuses diagnosed prenatally (I); neonates admitted to a treatment centre (II); and population-based studies (III). Population-based studies were defined as studies based on registry data, or studies intended to cover all cases in a defined geographical area and time span by use of vitality and hospital records. Category II only included studies of CDH patients who were symptomatic within the first 24 hours of life.

Outcomes assessed in the review
The outcomes were total, pre- or postnatal mortality rates. Total mortality rate was defined as any death in utero or postnatally. This excluded termination of the pregnancy. Postnatal mortality was reported as either neonatal mortality or deaths before discharge from hospital.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data were extracted on prenatal diagnosis, presence of associated major malformations, side of hernia, timing of surgery, termination of the pregnancy, intra-uterine foetal demise and postnatal deaths.
Methods of synthesis
How were the studies combined?
Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated and pooled, where appropriate, according to Normand (see Other Publications of Related Interest no. 1), then checked using the methods of Mantel-Haenszel (see Other Publications of Related Interest no. 2).

How were differences between studies investigated?
A chi-squared test was performed. A P-value of less than 0.05 was considered significant.

Results of the review
Fifty-one articles fulfilled the inclusion criteria: 17 studies (676 participants) were category I, 24 (1,609 participants) were category II and 10 (695 participants) were category III. For the assessment of the effect of pre- versus postnatal diagnosis, only 13 category II studies (812 participants in total) were included in the analysis.

The pooled visible postnatal mortality rate was 44.6% (range: 9.3 to 79.0) in CDH patients admitted to a centre for neonatal treatment. The pooled postnatal visible mortality rate was significantly higher (P<0.001) among prenatally diagnosed patients (51.0%) compared with postnatally diagnosed patients (37.2%) (pooled OR 1.9, 95% CI: 1.4, 2.8). The chi-squared test for heterogeneity showed no significant differences between the 13 studies included in the analysis (P=0.77).

Five studies reported total mortality rates excluding termination of the pregnancy. This was significantly higher (P=0.02) among prenatally diagnosed malformations (60.4%) than those diagnosed postnatally (39.6%) (OR 3.6, 95% CI: 1.9, 7.1). The chi-squared test for heterogeneity showed no significant differences (P=0.17).

The effect of the timing of surgery on mortality rate was not reported in any of the category I studies. Seven category II studies compared early with delayed surgery. With the exception of one prospective randomised study, all of the studies were historical comparisons. The pooled postnatal mortality rate was 42.9% for delayed surgery and 47.7% for early surgery, but this was not statistically significant (pooled OR 0.84, 95% CI: 0.62, 1.14). The prospective study showed a greater postnatal mortality rate associated with early (54%) versus late surgery (43%) (P>0.5).

Authors' conclusions
Prenatal diagnosis of CDH, presence of associated major malformations, and study population have a major influence on mortality rates. The very high mortality rate in studies with a prenatal diagnosis of CDH should be taken into account in prenatal counselling.

CRD commentary
This study was based on clear inclusion criteria and a reasonable search of the literature. However, only articles published in English were included and this may lead to publication bias, as the authors acknowledged in their discussion of the review's findings. In addition, no details of the number of reviewers involved in the study selection and data extraction processes, and how these processes were performed, were provided. Consequently, no comment can be made about the risk of bias with regards to the review methodology.

A variety of studies were included in the review. Some details of the studies were tabulated, but there was very little information on the study design, nature and accuracy of the diagnostic test, study setting and the participants. In addition, the validity of the studies was not assessed. A statistical test for heterogeneity was performed before the studies were pooled statistically, but some studies might have been pooled despite evidence of clinical heterogeneity. Based on the limited information provided, the analysis would appear to be valid. The authors also discussed a number of issues and problems associated with the review. The authors’ conclusions and implications for practice appear reasonable given the data presented, but should be viewed with caution considering the limitations of the review.

Implications of the review for practice and research
Practice: The authors stated 'the most striking finding in our study is the increased mortality rate found across study categories in patients with prenatal diagnosis. This knowledge should be taken into consideration when prenatal counselling is undertaken, and the relative high prevalence of associated major malformations should be considered both during prenatal examination of these foetuses and when counselling the parents'.

Research: The authors did not state any implications for further research.

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