Termination of pregnancy for fetal anomaly after 23 weeks of gestation: a European register-based study

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Accepted 26 January 2010.

Objective To determine the prevalence of termination of pregnancy for fetal anomaly (TOPFA) after 23 weeks of gestation in European countries, and describe the spectrum of anomalies for which late TOPFA is recorded.

Design Population-based study.

Setting Twelve European countries.

Population Nineteen registries of congenital anomaly in 12 European countries between 2000 and 2005. The number of total births covered was 2,695,832.

Methods TOPFAs in singleton pregnancies from the European Surveillance of Congenital Anomalies and Twins (EUROCAT) database.

Main outcome measures The prevalence of TOPFA and type of anomaly.

Results There were 10,233 TOPFAs, 678 (6.6%) of which were performed at 24 weeks or more. The rate of TOPFA before 24 weeks was 3.4 per 1000 births, at 24–25 weeks 0.14 per 1000 births and at 26 weeks or more 0.11 per 1000 births. There was significant variation in the prevalence of TOPFA at ≥24 weeks between countries (P < 0.001), with all countries in the range 0–0.55 per 1000 births, except France (Paris) at 2.65 per 1000 births. The large majority of late TOPFAs had a gestational age of 24–27 weeks (516/678, 76%). The proportion of TOPFAs from 24 weeks or more varied by type of anomaly, with 4% of all TOPFAs for chromosomal anomalies and 9% of all TOPFAs for nonchromosomal anomalies resulting in late TOPFA (P < 0.001). For transposition of the great arteries, single ventricle, hypoplastic left heart and hydrocephaly, the percentage of late TOPFA was 12–23%. The median time interval between diagnosis and late TOPFA was 2 weeks for most anomalies, but longer (≥5 weeks) for diaphragmatic hernia, omphalocele, arthrogryposis multiplex and Turner’s syndrome.

Conclusion Late TOPFA is rare in Europe, and varies in prevalence between countries. Compared with earlier TOPFA, late TOPFA is more often performed for a nonchromosomal isolated major structural anomaly and less often for a fetus with a chromosomal syndrome or multiple anomalies.

Keywords Fetal anomaly, termination of pregnancy.
There are few published data on the prevalence of TOPFA at a GA of 24 weeks or more, beyond the viability limit and the type of anomalies diagnosed in these pregnancies. A French study described the termination of pregnancy after 12 weeks of gestation from 1989 to 2000 for all fetal and maternal indications. In 74% of all terminations, the indication was fetal anomaly (39% with structural malformations and 35% with chromosomal anomalies). Although the percentage of TOPFA after 24 weeks was stable over time, an increasing prevalence of late TOPFA reflected an increase in the prevalence of all TOPFA. A British study from 1995 to 2004 found that 8.4% of TOPFAs were performed with a GA of 24 weeks or more.

In this article, we determine the prevalence of TOPFA from a GA of 24 weeks in 19 regions in 12 European countries in which TOPFA is legal, and describe the spectrum of congenital anomalies for TOPFA.

Materials and methods

The study was based on routinely collected data from 19 European Surveillance of Congenital Anomalies and Twins (EUROCAT) registries in 12 European countries in which TOPFA is legal: Austria (Styria), Belgium (Hainault and Antwerp), Denmark (Odense), France (Paris), Germany (Saxony-Anhalt), Italy (Tuscany, Emilia-Romagna, Campania), the Netherlands (Groningen), Norway, Portugal (South Portugal), Switzerland (Vaud), Ukraine, and England and Wales (East Midlands & South Yorkshire, Northern England, Thames Valley, Wales and Wessex).

The study years were 2000–05, except for France and Ukraine where only 2005 data were available. The total number of registered births (live and stillbirths) covered in the study period for the 19 regions was 2,695,832.

The EUROCAT registries are all population based, recording all live births, stillbirths and TOPFA with congenital anomaly in their populations. A description of the geographically defined populations and the methods of case ascertainment for EUROCAT is given at www.eurocat-network.eu.

The registries are based on multiple sources of information, including hospital records, birth and death certificates, and postmortem examinations, and include information about live births, fetal deaths at GA ≥ 20 weeks and terminations of pregnancy after prenatal diagnosis of fetal anomaly at any GA (TOPFA). All structural malformations, syndromes and chromosomal anomalies are included in the database, except for minor anomalies specified on a list for exclusion. Case information includes type of birth (live birth, fetal death or termination of pregnancy), GA at prenatal diagnosis (at first suspicion or positive test) and GA at delivery (birth or termination). Up to eight anomalies per case and syndrome, if present, are coded according to the International Classification of Diseases v9 (ICD9)/British Paediatric Association (BPA) or ICD10/BPA, and the cases are allocated to subgroups of anomalies based on the ICD codes. All cases not diagnosed with a chromosomal anomaly are classified as nonchromosomal, and this includes cases that have not been karyotyped. All TOPFA cases with GA ≥ 24 weeks with multiple anomalies (more than one organ system, excluding associations, chromosomal anomalies and monogenic syndromes) were identified using the EUROCAT multiple anomaly computer algorithm, followed by manual review by a panel of medical geneticists.

All terminations of pregnancy in singletons only were included in the study. Data were extracted from the central database, and local registries then confirmed GA at termination for all TOPFA with a GA of 24 weeks or more.

We defined late TOPFA to be GA ≥ 24 weeks of gestation, because of general agreement on a viability limit at 24 weeks.

We calculated the prevalence of TOPFA at <24 and ≥24 weeks of gestation for each country (based on the corresponding registry data) with 95% Poisson exact confidence intervals (CIs); the denominators were the total number of births in the population base for the EUROCAT areas within each country. The proportion of terminations at <24 and ≥24 weeks of gestation were estimated with 95% binomial exact CIs for each country, as well as for the overall study population. For the latter, clustering by country was taken into account in the calculation of binomial Wald CIs. The median GAs at diagnosis and at termination, as well as the median difference between GAs at diagnosis and termination, were calculated with 95% linear interpolation binomial-based CIs.

Results

During the study period, there were 10,233 TOPFAs reported in singleton pregnancies. GA was unknown for 451 of these cases (4.4%). Among the 9,782 TOPFAs with known GAs, 5,396 (55%) were diagnosed with nonchromosomal anomalies and 4,386 (45%) were diagnosed with a chromosomal anomaly.

TOPFA with GA of less than 24 weeks accounted for 93% of all TOPFAs, a rate of 3.4 per 1000 births (range, 1.4–7.1 per 1000 births) (Table 1). TOPFA with GA ≥ 24 weeks accounted for 7% (678 cases).

Eleven countries performed TOPFAs at 24–25 weeks of gestation [prevalence, 0.14 per 1000 births (range, 0.03–0.97 per 1000 births)]. Ten countries reported TOPFA at 26 weeks of gestation or more [prevalence, 0.11 per 1000 births (range, 0.03–1.68 per 1000 births)]. The total rate of
TOPFA at 24 weeks or more varied from 0 to 2.65 per 1000 births in the 12 countries: the variation between countries was highly statistically significant \((P < 0.001)\) (Figure 1).

The large majority of late TOPFAs had a GA at 24–27 weeks (516/678, 76%) and 162 TOPFAs had a GA of 28 weeks or more (Figure 2).

For structural anomalies, 498/5396 (9%) of TOPFAs had a GA of 24 weeks or more, whereas, for cases with chromosomal anomalies, 180/4386 (4%) had a GA of 24 weeks or more \((P < 0.001)\).

The proportion of late TOPFA varied by type of anomaly (Table 2). Those that were difficult to diagnose by ultrasound (hydrocephalus, severe cardiac malformations)
had a higher proportion of late TOPFAs than those that were more easily seen on ultrasound, such as anencephalus and abdominal wall defects.

For chromosomal anomalies, the highest proportion of late TOPFAs was for trisomy 13, with 6.4% of all TOPFAs with a GA of 24 weeks or more (Table 3).

![Figure 2. Distribution of gestational age (GA) for termination of pregnancy for fetal anomaly (TOPFA) with GA from 24 weeks.](image-url)

**Table 2.** Number of terminations of pregnancy for fetal anomaly (TOPFAs) by selected types of nonchromosomal anomaly, proportion of TOPFAs with gestational age (GA) of 24 weeks or more, median GA at diagnosis and median GA at TOPFA.

<table>
<thead>
<tr>
<th>Congenital anomaly type*</th>
<th>Total TOPFA cases (n)</th>
<th>Percentage of anomalies with TOPFA ≥ 24 weeks (95% CI)</th>
<th>Median GA at diagnosis in weeks, TOPFA ≥ 24 weeks** (95% CI)</th>
<th>Median GA in weeks at TOPFA ≥ 24 weeks (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All anomalies excluding diagnosed chromosomal anomalies</td>
<td>5396</td>
<td>9.2 (8.5–10.0)</td>
<td>23 (23–23)</td>
<td>25 (25–25)</td>
</tr>
<tr>
<td>Anencephalus and similar</td>
<td>864</td>
<td>2.5 (1.6–3.8)</td>
<td>23 (22–24)</td>
<td>25 (24–28)</td>
</tr>
<tr>
<td>Encephalocele</td>
<td>180</td>
<td>2.2 (0.6–5.6)</td>
<td>24.5 (22–29)</td>
<td>26.5 (24–30)</td>
</tr>
<tr>
<td>Spina bifida***</td>
<td>754</td>
<td>7.3 (5.5–9.4)</td>
<td>23 (23–24)</td>
<td>25 (24–26)</td>
</tr>
<tr>
<td>Hydrocephaly***</td>
<td>560</td>
<td>14.3 (11.5–17.5)</td>
<td>23 (23–24)</td>
<td>26 (25–27)</td>
</tr>
<tr>
<td>Arhinencephaly/holoprosencephaly</td>
<td>138</td>
<td>12.3 (7.3–19.0)</td>
<td>24.5 (23–28)</td>
<td>26 (25–32)</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>976</td>
<td>12.2 (10.2–14.4)</td>
<td>23 (22–24)</td>
<td>25 (24–25)</td>
</tr>
<tr>
<td>Transposition of great vessels</td>
<td>51</td>
<td>15.7 (7.0–28.6)</td>
<td>22.5 (22–29)</td>
<td>24 (24–30)</td>
</tr>
<tr>
<td>Single ventricle</td>
<td>43</td>
<td>23.3 (11.8–38.6)</td>
<td>23.5 (22–29)</td>
<td>25 (24–28)</td>
</tr>
<tr>
<td>Atrioventricular septal defect</td>
<td>88</td>
<td>13.6 (7.2–22.6)</td>
<td>22 (20–23)</td>
<td>24.5 (24–26)</td>
</tr>
<tr>
<td>Hypoplastic left heart</td>
<td>282</td>
<td>12.1 (8.5–16.4)</td>
<td>23 (22–24)</td>
<td>24 (24–25)</td>
</tr>
<tr>
<td>Oesophageal atresia</td>
<td>38</td>
<td>10.5 (2.9–24.8)</td>
<td>23.5 (19–28)</td>
<td>26 (24–29)</td>
</tr>
<tr>
<td>Diaphragmatic hernia</td>
<td>95</td>
<td>9.5 (4.4–17.2)</td>
<td>21 (17–29)</td>
<td>26 (24–29)</td>
</tr>
<tr>
<td>Gastrochisis</td>
<td>72</td>
<td>2.8 (0.3–9.7)</td>
<td>23.5 (23–24)</td>
<td>25 (24–26)</td>
</tr>
<tr>
<td>Omphalocele</td>
<td>234</td>
<td>3.4 (1.5–6.6)</td>
<td>18 (13–33)</td>
<td>24.5 (24–34)</td>
</tr>
<tr>
<td>Bilateral renal agenesis</td>
<td>216</td>
<td>8.8 (5.4–13.4)</td>
<td>23 (22–25)</td>
<td>25 (24–26)</td>
</tr>
<tr>
<td>Arthrogryposis multiplex congenita</td>
<td>64</td>
<td>14.1 (6.6–25.0)</td>
<td>20.5 (18–25)</td>
<td>26 (25–26)</td>
</tr>
<tr>
<td>Thanatophoric skeletal dysplasia</td>
<td>74</td>
<td>1.4 (0.03–7.3)</td>
<td>24 (24–24)</td>
<td>24 (24–24)</td>
</tr>
<tr>
<td>Monogenic syndromes + microdeletions</td>
<td>250</td>
<td>9.2 (5.9–13.5)</td>
<td>24 (21–26)</td>
<td>26 (25–28)</td>
</tr>
</tbody>
</table>

CI, confidence interval.

*Cases with more than one major anomaly may be presented in more than one group.

**GA at diagnosis not available for 17% at late TOPFAs.

***Cases with spina + hydrocephalus counted in the spina bifida subgroup only.
The types of anomaly diagnosed for all 678 TOPFAs with a GA of 24 weeks or more are presented in Table 4. Twenty-seven percent of all late TOPFAs were caused by chromosomal anomalies and 73% were caused by major structural anomalies. Ten percent of late TOPFAs were for multiple anomalies, 6% for monogenic syndromes and the remaining 57% for isolated major structural anomalies.

For all 678 TOPFAs with a GA of 24 weeks or more, the median GA at diagnosis was 23 weeks and the median GA at TOPFA was 25 weeks. For four anomalies, the median time interval between diagnosis and late TOPFA was more than 5 weeks: diaphragmatic hernia, omphalocele, arthrogryposis multiplex and Turner’s syndrome.

**Discussion**

In our study population of 12 European countries in which TOPFA is legal, we found, on average, approximately one late TOPFA per 4000 births (0.25 per 1000 births) for the period 2000–05. More than one-half of these terminations of pregnancy were performed following the diagnosis of a major anomaly of a single organ system. We do not know from our registry data whether the anomaly diagnosed was the sole reason for the termination. There may also have been other conditions contributing to a poor prognosis, such as severe fetal growth restriction, severe hydrops, severe oligohydramnios or additional maternal factors.

The rate of TOPFA with a GA of 24 weeks or more varied considerably between countries, from less than 0.1 per 1000 births in the Netherlands (Groningen), Denmark (Odense) and Norway, to 2.65 per 1000 in France (Paris), with all countries other than France having rates under 0.6 per 1000. There was a poor relationship between the prevalence of early terminations and the prevalence of late terminations—a point illustrated by the fact that both France (Paris) and Switzerland (Vaud) showed high rates of termination before 24 weeks (6.8 and 7.1 per 1000, respectively), whereas Paris had a much higher rate of termination after 24 weeks than Vaud. Several other studies have reported previously a high prevalence of late TOPFA in France. The variations in TOPFA rates in Europe have been reported previously.

In Paris, the second trimester anomaly scan tends to be performed later than in other European countries. An earlier analysis of EUROCAT registry data showed the median GA at diagnosis for structural anomalies was 22 weeks in...
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Paris, compared with 19–20 weeks in registries in Belgium, Italy and the UK. As our data suggest that the median time from prenatal diagnosis to termination is 2 weeks, having a relatively late GA for the anomaly scan would result in more TOPFA after 24 weeks. Nevertheless, Paris also had a higher TOPFA rate from 26 weeks of gestation, suggesting a higher acceptability of late termination in this population. Paris, like some but not all European countries, also has a recommended third trimester scan.

There are some limitations to our data. The areas covered by EUROCAT are not necessarily representative of the entire country. Furthermore, it is possible that some late TOPFAs were recorded in the EUROCAT registers as stillbirths or live births (i.e. early birth inductions) rather than TOPFA, depending on local medical practice. In some areas, TOPFA performed outside the registry area may not be known to the registry, as in Saxony-Anhalt, Germany. This may also be the case in countries with an upper GA limit for TOPFA. In the Ukraine, the legal limit for TOPFA was 28 weeks during the study period (2005), but was reduced to 22 weeks in 2006.

Terminations after 24 weeks, although a small proportion of all TOPFAs, nevertheless constitute a potentially large proportion of perinatal deaths or stillbirths. Countries vary in terms of the legal requirement to register late TOPFA as a live or stillbirth, and in terms of whether perinatal mortality associated with TOPFA can be distinguished from other perinatal mortality. The Models of Organising Access to Intensive Care for very preterm babies (MOSAIC) study published termination of pregnancy rates for European regions for a GA of 22–31 weeks for 2003 for any indication (fetal and maternal). The data sets are not completely comparable but, given the high rates of termination of pregnancy after 22 weeks in the MOSAIC study, it may be that there is some under-reporting of TOPFA as stillbirths in the current study. Until there is harmonisation of recording practices, late TOPFA creates difficulties in the interpretation of the variation between countries in stillbirth and perinatal mortality rates. On the one hand, late TOPFA may decrease perinatal mortality rates when it is not civilly registered, but may also increase perinatal mortality rates when it is performed for nonlethal anomalies and is civilly registered.

The spectrum of anomalies in late TOPFA differs from that of early TOPFA, with a higher proportion of structural anomalies and a lower proportion of chromosomal anomalies. We also found that 57% of TOPFAs with a GA of 24 weeks or more are performed after prenatal diagnosis of an isolated major structural anomaly, and the proportion of multiple anomalies was only 10% (Table 4). The proportion of multiple malformed cases is lower than that found in two other studies from single centres. Single-centre studies may be biased towards tertiary referral centres.

Certain anomalies were particularly likely to be associated with late termination, including single ventricle, transposition of the great vessels, arthrogryposis multiplex and hydrocephaly, for which more than 14% of all terminations were at 24 weeks or later. The distribution of the isolated major anomalies in late TOPFA, with a high proportion of cerebral anomalies in our European multicentre study, is comparable with that of other regional studies published in France (Isere, Paris), UK (Northern Region) and Israel. Two of these studies presented data on third trimester terminations (GA ≥ 28 weeks).

The median time interval from diagnosis to termination was 2 weeks. A reasonable time interval is needed between diagnosis and termination of pregnancy to allow referral to specialists and prenatal counsellors, to wait for karyotype results, to allow parents to reach an informed decision, and to obtain permission for termination from a committee or more than one doctor. In four anomalies, we found a median time interval of more than 1 month from prenatal diagnosis to termination: diaphragmatic hernia, omphalocele, arthrogryposis multiplex and Turner’s syndrome. Turner’s syndrome is an example in which termination is most frequently performed when severe fetal hydrops is diagnosed late in gestation. In the case of diaphragmatic hernia, liver herniation suggests a poor prognosis and may influence the decision to terminate. Other indications, such as lung hypoplasia in diaphragmatic hernia and fetal akinesia in arthrogryposis late in pregnancy, may also influence the prognosis and the decision to terminate.

It was not our purpose in this article to discuss the ethical or psychological aspects of late termination. We note, however, that the general consensus is that ethical and psychological acceptability of TOPFA is greater the earlier in pregnancy in which it is performed.

There is a balance to be reached, which takes into account cultural and ethical considerations, between having an earlier anomaly scan policy which allows earlier TOPFA or a later scan policy with a higher and sometimes more accurate prenatal detection rate, but resulting in later TOPFA. There may be situations in which it is necessary to follow the development of an anomaly to see if the fetus deteriorates in the weeks following a diagnosis, for example after a prenatal diagnosis of less severe hydrocephalus. The availability of late TOPFA may allow parents to make a decision on the basis of more accurate information from a later investigation.

Addendum

TOPFA rates and rates before and after 20 weeks of gestation, for the most recent 5 years, can be found at the EUROCAT website: www.eurocat-network.eu. These data are updated annually.
Disclosure of interest
None.

Contribution to authorship
EG defined the research question, wrote the study description, wrote the paper, contacted local registries and is the corresponding author.

BK performed the statistical analysis, revised all versions of the paper and gave final approval.

ML wrote the study description, managed the data, performed statistical analysis, contacted local registries, revised all versions of the paper and gave final approval.

TB wrote the study description, revised all versions of the paper and gave final approval.

HD defined the research question, revised all versions of the paper and gave final approval.

Details of ethics approval
This was a central database study based on data from local registries. Ethics approval was performed by local registries.

Funding
EUROCAT is funded by the European Union Public Health Programme.

Acknowledgements
EUROCAT is funded by the European Union Public Health Programme.

Concerning Thames Valley Registry and Northern England: This paper reports an independent study funded by the Healthcare Quality Improvement Partnership (Department of Health). The views expressed are not necessarily those of the Department. The East Midlands and South Yorkshire Congenital Anomaly Register is funded by the primary care trusts covering the described populations. We acknowledge the fund providers of all EUROCAT registries as detailed under www.eurocat-network.eu.

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