OBSTETRICS

Fetopathologic examination for early termination of pregnancy: dogma or necessity?

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OBJECTIVE: Our objective was assessment of fetopathological examination after termination of pregnancy (TOP) for fetal anomalies with normal karyotype <17 weeks of gestation.

STUDY DESIGN: This was a multicenter retrospective study. Records of TOP for fetal anomalies with normal karyotype were analyzed. Primary outcomes were modifications of genetic counseling and management of next subsequent pregnancies. Medical TOPs were compared with surgical TOPs.

RESULTS: In all, 59 pregnancies were included (30 aspirations, 29 inductions). Fetopathological examination modified genetic counseling for 22 patients: 62% for the medical induction group vs 13% in the vacuum aspiration group ($P < .001$). Management of subsequent pregnancies was modified in 17% in the medical induction group vs 3% in the aspiration group ($P = .06$).

CONCLUSION: Fetopathological examination for early TOP with normal karyotype is relevant, especially when an intact fetus is examined. Thanks to it, genetic counseling is often modified, as is management of the next pregnancy. Medical procedures should be preferred to surgical procedures.

Key words: fetopathological examination, genetic counseling, medical induction, termination of pregnancy, vacuum aspiration

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In most countries the first ultrasound screening during pregnancy is performed between 11-14 weeks of gestation (WG). Thanks to progress in ultrasound, more fetal malformations that used to be diagnosed later are now detected during this first trimester, such as cephalic pole malformations, bone anomalies, hygromas, anomalies of the anterior wall, and others, including multiple malformations. In France, when such anomalies are suspected, the patient is referred to a prenatal diagnosis center. When severe malformations are confirmed by an experienced sonographer, termination of pregnancy (TOP) can be requested by the parents and accepted by the prenatal diagnosis center, according to French law. In the case of fetal malformations related to an abnormal karyotype, vacuum aspiration is proposed. However, when the fetal karyotype is normal, medical induction is usually recommended so that an intact fetus is available for fetopathological examination. Some patients though ask for vacuum aspiration because the procedure is believed to be simpler. Although autopsy is known to offer a real benefit after 18 WG,[1-5] its value for genetic counseling and management of the next pregnancy has never been studied for earlier TOP. Is there a difference in autopsy quality between aspiration and induction? To answer this question we carried out a retrospective multicenter study.

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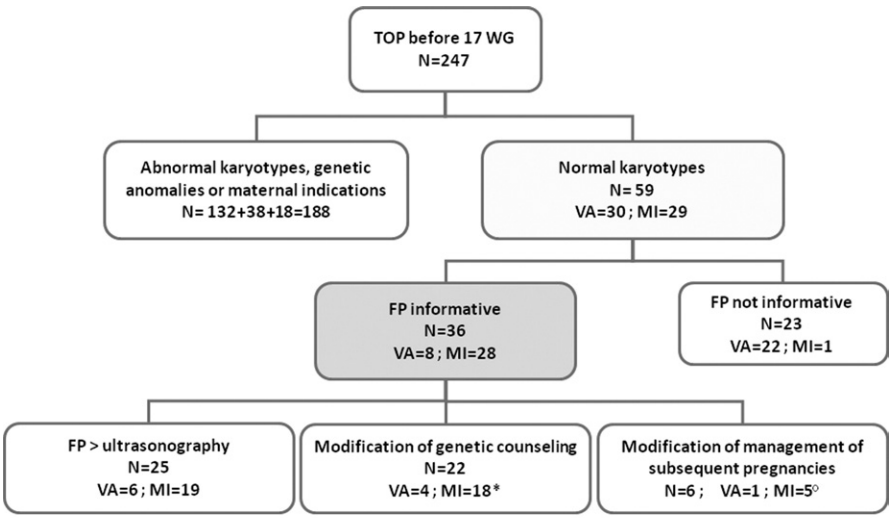
Materials and Methods

This retrospective study concerning the period from January 2006 through December 2008 was carried out in 2 prenatal centers in Paris (Port-Royal Saint-Vincent de Paul Hospital and Robert Debré Hospital). The aim of the study was to assess the value of fetopathological examination in early TOP. Does it complement ultrasound examination, and modify genetic counseling and management of the next pregnancy? Does the method used for TOP change the value of the autopsy and the risk incurred by patients?

To answer these questions, we retrieved from the prenatal diagnosis center registers all medical records of pregnancies that ended in TOP <17 WG. We excluded TOPs performed because of an abnormal karyotype, a genetic abnormality already known in the family (eg, sickle cell anemia, hemophilia, myopathy, metabolic disease), or a maternal indication (eg, cancer, psychiatric or cardiac reasons). In both last groups (genetic disorders and maternal diseases) the early scans were normal.

All patients underwent first ultrasound screening between 11-14 WG. All

FIGURE 1
Impact of fetopathological examination before 17 WG



FP, fetopathological examination; *MI*, medical induction; *N*, number; *VA*, vacuum aspiration; *WG*, weeks of gestation.

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malformations were suspected during this screening. Gestational age was calculated using the crown-rump length. All reports on fetal ultrasound examinations, laboratory tests, and fetal samples were pooled. All data concerning management of TOP and postabortum were studied. The detailed fetopathological reports were analyzed, as were genetic records. Data were then analyzed by a board of experienced practitioners including a sonographer, a fetopathologist, a geneticist, and an obstetrician.

The primary outcomes were to determine the effects of fetopathological examination on genetic counseling and on management of the next pregnancy. Fetopathological data were considered uninformative when the fetus was so fragmented that organs could not be identified. Secondary outcomes were to know whether fetopathology identifies malformations missed by ultrasound, to review major and minor maternal complications, and to analyze the duration of hospital stay.

Patients chose the method for TOP after medical counseling. They were offered both options, but medical induction was recommended.

In the case of vacuum aspiration, the patient received 200 mg of mifepristone orally 2 days before the surgical aspiration. On the day of TOP, the patient was admitted early in the morning and received 400 μg of misoprostol vaginally at least 2 hours before the aspiration, which was performed under general anesthesia in the operating room. Cervical dilatation was increased mechanically to a diameter of 12 mm using Hegar dilators. Evacuation was done with a cannula connected to a suction pipe under ultrasound guidance.

In the case of medical induction, the patient received 200 mg of mifepristone orally 2 days before the induction. She was admitted the evening before the induction. Laminaria were used in 1 center (Robert Debré Hospital). Early in the morning the patient was taken to the delivery room and given 400 μg misoprostol vaginally every 3 hours under epidural anesthesia.

The fetopathological examinations were carried out according to standardized protocols that were the same in both centers. With the patient's consent, the fetus or vacuum aspiration products, in a fresh state, were sent to the laboratory as rapidly as possible. The vacuum aspiration products were washed, and then fixed overnight in 4% formol. The macroscopic examination consisted of separating different elements (decidua, placenta, cord, fragments, and fetal organs). For the identifiable elements, we carried out a morphological examination, took digitized pictures and radiographs (Faxitron cabinet x-ray system-Faxitron series; Faxitron Bioptics, Lincolnshire, IL), and performed a histologic examination.

The autopsy protocol for a whole fetus involved routine radiological examination followed by standardized x-rays (whole body, face, profiles). The macroscopic examination concerned the face, limbs and extremities, and anterior abdominal wall. All organs were then dissected. Samples of the brain, muscles, and ribs were collected routinely; the marrow and eyes were studied depending on the context. These organs were examined histologically. Macroscopic and histologic examinations of the extraembryonic structures, placenta, and membranes were routine.[6]

TOP was divided into 5 groups according to indication: anomalies of the cephalic pole, bone anomalies, hygromas, anomalies of the anterior wall, and others, including multiple malformations.

Results were analyzed using the χ^2 test.

RESULTS

During the 36 months of the study, there were 22,386 deliveries in the 2 centers and 247 patients underwent TOP <17 WG. This corresponds to 29% of all TOP (n = 848) during this period. In all, 188 patients were excluded from the study: 18 who had undergone TOP for maternal medical reasons, 38 because of a genetic disease in the family, and 132 for an abnormal karyotype. Most fetuses with an abnormal karyotype had trisomy 21 (n = 59) or trisomy 18 (n = 40).

Fifty-nine pregnancies were included (Figure 1). All fetuses had a normal karyotype and isolated or multiple anomalies detected by ultrasonography and of sufficient severity for the prenatal diagnosis center to agree to the parents' request for TOP, in accordance with French law.

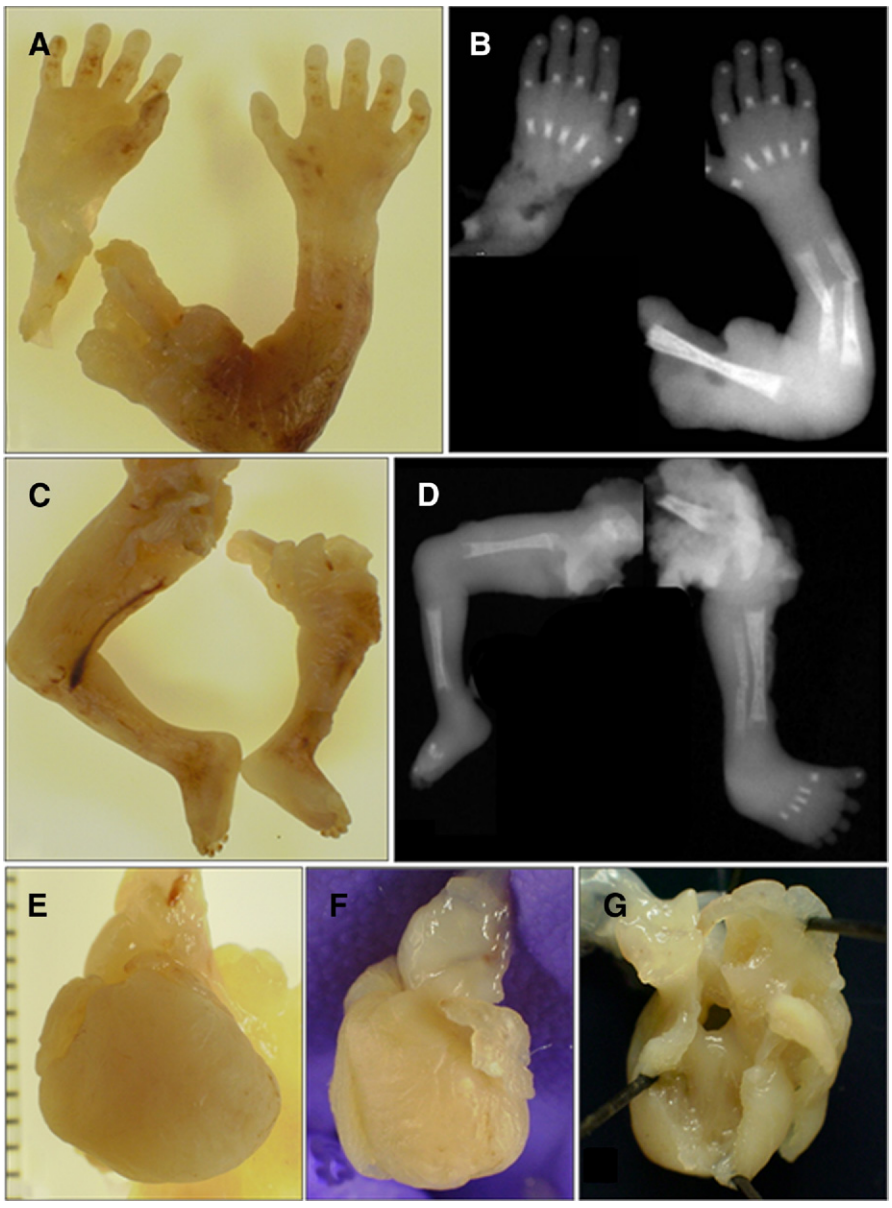
Thirty patients underwent vacuum aspiration (average gestational age 13.5 WG) and 29 medical induction (average gestational age 15.3 WG). Indications and methods for TOP are shown in Table 1.

The fetopathological examinations were uninformative in 23 of 59 cases (39%): 22 vacuum aspiration products were too fragmented to be analyzed; 1 fetus with a hygroma was examined 2 days after medical induction, the state of desiccation was advanced, cutaneous edema could not be found and the rest of the findings were normal. Thirty-six examinations were informative: 8 vacuum aspirations and 28 medical inductions. Figures 2 and 3 show examples of fetopathological examination after vacuum aspiration and medical induction, respectively.

The results are shown in Table 2.

Of the 36 informative examinations, 25 (42%) autopsies revealed more pathological details than ultrasonography (19 [65%] in the medical induction group vs 6 [20%] in the vacuum aspiration group). In 22 (37%) patients, these new details affected genetic counseling (18 [62%] in the medical induction group and only 4 [13%] in the vacuum aspiration group). Autopsy after medical induction significantly improved genetic counseling compared with aspiration ($P < .0001$). Management of the next pregnancy was modified for 6 patients, ie, 5 (17%) in the medical induction group vs 1 (3%) in the vacuum aspiration group ($P = .06$). These 6 cases are detailed in Table 3. Details of the 22 cases in which fetopathological examination affected genetic counseling are available in the Appendix (Supplementary Tables 1-5).

FIGURE 2
Fetopathological examination after vaccuum aspiration



A, Macroscopy of upper limbs. **B,** Radiography of upper limbs showing fractures resulting from vacuum aspiration. **C,** Macroscopy and **D,** radiography of lower limbs. **E,** Anterior view of heart: small left ventricule with advanced heart to right ventricule. **F,** Left exterior view of heart. **G,** Interior view of heart with interventricular communication.

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Maternal complications

The mean length of hospital stay was 1.29 days in the vacuum aspiration group, with 24 outpatients. One patient stayed 5 days because of a uterine perforation and 3 had to stay 1 night because they entered the operating room too late to go home on the same day. The mean length of hospital stay was 2.44 days in the medical induction group.

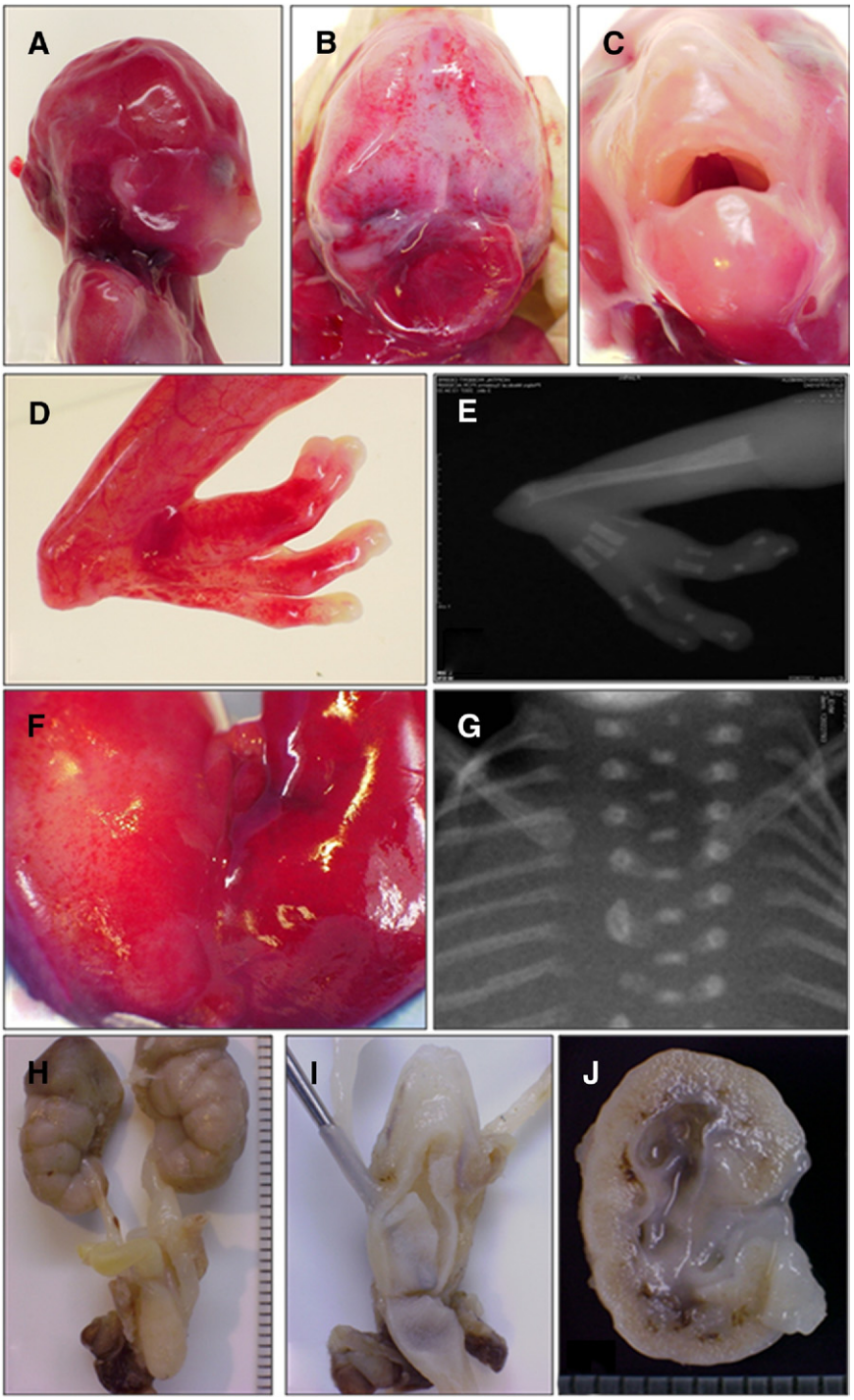
Six patients undergoing medical induction required vacuum aspiration after delivery because of placenta retention (ie, 20%). One vacuum aspiration resulted in cervical injury.

A uterine perforation occurred in the vacuum aspiration group, with intraabdominal passage of the aspiration product. Exploratory laparoscopy and then laparotomy were needed to evacuate the waste and suture the anterior uterine wound (Table 4).

Comment

The study highlights the value of the fetopathological examination for early TOP when the fetal karyotype is normal. The autopsy is much more informative

FIGURE 3
Fetopathological examination after medical abortion at 15 WG



A, Profile with retrognathism, microcrania, and occipital encephalocele. **B,** Occipital encephalocele. **C,** Face with cleft palate. **D,** Macroscopic radial club hand. **E,** Club hand, radial agenesis, syndactyly. **F,** Imperforate anus. **G,** Vertebral abnormality. **H,** Right pyelourethral dilatation. **I,** Ureterocele. **J,** Pyelocaliceal dilatation.

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when the fetal body is preserved. In the medical induction group, the autopsy modified genetic counseling in 62% of cases and management of the next pregnancy in 17% of cases, vs 13% and 3%, respectively, in the vacuum aspiration group.

The results in the medical induction group are comparable to those found >18 WG. In the literature, autopsy is said to have an impact on genetic counseling in 18-51% of cases.[1-5] In our study, autopsy was possible after vacuum aspiration, but fetal fragmentation greatly limits the analysis. The patient should be informed of the potential loss of information if vacuum aspiration is chosen.

The fetopathological examination of an intact fetus is possible ≥13 WG. It is, however, important to emphasize that neither the morphogenesis nor the histogenesis are finished. Thus, some elements of a congenital syndrome can be missing. For example, concerning the encephalon, corpus callosum agenesis cannot be diagnosed <16-18 WG, nor can anomalies of the pyramidal tract (eg, microcephaly, hydrocephalus). Moreover, brain lesions in Bourneville disease only occur later in pregnancy, usually in the third trimester.

We can assume that there might be some bias because this is not a randomized study. Several factors reduce bias based on location. The 2 centers are very similar in the way they manage early TOP. The usual counseling and the recommendation for medical induction, the quality of ultrasound screening, the protocols for vacuum aspiration and for medical induction, the fetopathological examination are quite similar. We cannot completely exclude potential bias due to the choice of the procedure. Nevertheless, Table 1 shows that the between-group difference is in gestational age. Vacuum aspiration is chosen more often when the term is early. Nevertheless, indications for TOP were similar in the 2 groups. This reduces bias in the assessment of autopsy.

Although the data are somewhat limited, the available evidence indicates that, compared with vacuum aspiration, medical TOP is associated with potentially increased risk for maternal complications such as retained products of conception,

TABLE 1
Indications and methods used

Indication	Vacuum aspiration (n = 30)	Medical abortion (n = 29)	Total (n = 59)
Anomalies of cephalic pole	12	12	24
Bone anomalies	5	5	10
Hygroma	6	4	10
Anomalies of anterior wall	3	5	8
Multiple malformations or others	4	3	7

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procedure failure, and hemorrhage. We noted a few complications. Only 1 major complication occurred during vacuum aspiration. But this is a retrospective study and minor complications may have been underestimated. In our study, medical induction resulted in slightly less complete evacuation, bleeding, and infections. Preventive measures can limit the risk of these complications.[7-9] The surgical method is acceptable even >15 WG.[7-9] Finally, there are more persuasive arguments in favor of medical induction for TOP when the fetal karyotype is normal, but discussion with the patient is needed to allow her to weigh the risks and benefits of the 2 methods.

Assessment of the psychological repercussions is challenging, and several parameters should be taken into account. The method used is certainly not the only parameter to assess. Doubt about the correctness of the diagnosis and lack of knowledge about the disease are predictors for adverse outcome after TOP for fetal anomalies.[10] We can presume that the answers given by the autopsy also play a role in the way the patient can psychologically overcome TOP. It is important to consider the way that the autopsy impacts on diagnosis, etiology, and especially genetic counseling and management of subsequent pregnancies. This assessment needs further studies.

To sum up, management of early TOP when the karyotype is normal has to find a balance between obtaining the most accurate diagnosis possible and preserving the

TABLE 2
Value of fetopathological examination depending on method used

Method used	Not informative	Informative	Superior to ultrasonography	Modification of genetic counseling	Modification of management of subsequent pregnancies
Vacuum aspiration (n = 30)	22	8	6	4	1
Medical abortion (n = 29)	1	28[a]	19	18[a]	5[b]
Total (n = 59)	23	36	25	22	6

Not informative = results of fetopathological examinations were considered not informative when report concluded: fragmented fetus only some tissues of which were identifiable, without more information. Informative = several organs were identified and analyzed.

[a] $P < .0001$; [b] $P < .06$.

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TABLE 3
Cases in which fetopathological examination modified management of subsequent pregnancies

Case	Route	Term (WG)	Data of ultrasonography examination	Karyotype pre or post* TOP	Data of fetopathological examination complementing ultrasonography data	Genetic counseling	Actions to be taken for next pregnancy
2	E	15	Short upper limbs and nuchal translucency 3,2 mm	46, XY*	Brachymelia, short and incurved radius and ulna, oligodactylies	Ulnar-mammary syndrome, TBX3 gene	Genetic study
4	E	17	Short and incurved long bones, retrognathism, hexadactyly and hygroma at 4,3 mm	46, XX	Hypoplastic scapulae, iliac wings, fractures, very incurved tibias and fibulas	Camptomelic dysplasia, SOX 9 gene	Genetic study
15	A	13	Exencephaly	46, XY	Exencephaly, APSO, single umbilical artery and meconium calcification	Possible recurrence	Cardiac ultrasonography
20	A	13	Hygroma at 5 mm and anasarca	46, XY*	Hepatic calcifications, adrenal cytomegalies, alignment of heart valves	Possible recurrence	Cardiac ultrasonography
21	E	14	Hygroma at 6 mm	46, XX	Müllerian agenesis, wrongly segmented vertebral column, hypoplasia of left heart	Association MURCS	Oriented ultrasonography
22	E	15	Cystic hygroma	46, XY	Hygroma and bicuspid aortic valves with elongation of aortic isthmus	Heart disease	Cardiac ultrasonography

A, aspiration; *E*, evacuation; *MURCS*, Müllerian-renal-cervicothoracic somite abnormalities; *TOP*, termination of pregnancy; *WG*, weeks of gestation.

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TABLE 4
Maternal complications

Variable	Vacuum aspiration (n = 30)	Medical abortion (n = 29)	Total (n = 59)	*P* value
Patient age, y	32.5 ± 5.2	28.7 ± 4.9	30.8 ± 5.4	.002
Term of TOP (WG)	13.5 ± 0.9	15.3 ± 1.1	14.3 ± 1.3	.001
Duration of stay, d	1.3 ± 0.8	2.4 ± 0.7	1.8 ± 0.9	.005
Rate of general anesthesia	100%	3%	52%	.001
Minor complication[a]	1	6	7	NS
Major complication[b]	1	0	1	NS

NS, not significant; *TOP*, termination of pregnancy; *WG*, weeks of gestation.

[a] Retention, cervical injury; [b] Perforation with intraabdominal passage of aspiration product requiring laparoscopy then laparotomy.

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best obstetrical and psychological future for the patient. Medical induction seems to us preferable since it enables the more informative fetopathological examination, which in this study modified genetic counseling in 62% of cases and management of the next pregnancy in 17%. A prospective study is needed to assess the physical and psychological consequences of each method in these situations. ■

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Appendix

SUPPLEMENTARY TABLE 1
Fetopathological examination modified genetic counseling in TOP for limb abnormalities

Case	Route	Term	Data of the ultrasonographic examination	Karyotype pre or post* TOP	Data of the fetopathological examination complementing the ultrasonographic data	Genetic counseling	Actions to be taken for next pregnancy
1	E	15	Inactive lower limbs, short and incurvate femur	46, XY*	No fibulas, knee luxation, postaxial oligodactylies, hypospadias	Furhmann syndrome, AR, WNT7A gene	Genetic study
2	E	15	Short upper limbs and nuchal translucency 3.2 mm	46, XY*	Brachymelia, short and incurvate radius and ulna, oligodactylies	Ulnar-mammary syndrome, AR, TBX3 gene	Genetic study
3	E	16	Spondylocostal dysplasia and nuchal translucency 2.7 mm	46, XX	Spondylocostal dysplasia and caracteristic bone abnormalities	Jarcho Lewin syndrome, AD, no gene	
4	E	17	Short and incurvate long bones, retrognatism, hexadactyly and hygroma at 4.3 mm	46, XX	Scapula hypoplasia, iliac wings, fissure fractures, very incurvate tibias and fibulas	Campomelic dysplasia, AR, SOX 9 gene	Genetic study
5	E	17	Osteochondrodysplasia with narrow chest and abnormalities to the posterior cranial fossa	46, XY	Narrow chest, short ribs, histologic aspect of a type II thanatophoric dWGrfism	Thanatophoric dwarfism, AD, FGFR3 gene	

E, evacuation; *TOP*, termination of pregnancy.

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SUPPLEMENTARY TABLE 2

Fetopathological examination modified genetic counseling in the TOP for megacystis or multiple malformations

Case	Route	Term	Data of the ultrasonographic examination	Karyotype pre or post* TOP	Data of the fetopathological examination complementing the ultrasonographic data	Genetic counseling	Actions to be taken for next pregnancy
6	E	15	Megacystis	46, XY*	Megacystis, microcolon, parietal muscular dystrophy	Megacystis Microcolon	
7	A	14	Megacystis	46, XY*	Megacystis by urethra atresia	Occasional accident, no recurrence	
8	E	16	Megacystis, oligohydramnios, 2 hyperechoic kidneys	46, XX*	Urogenital sinus, hypoplastic uterus, blind ureteral fistula, urethra atresia	Urogenital association, possible recurrence	
9	E	14	Anencephalia, laparoschisis and median cleft	46, XX*	Anencephalia, median cleft, laparoschisis and amniotic bands	Amniotic band disease	
10	E	15	Posterior meningo-encephalocele, hyperechoic kidneys, radial clubhand	46, XX	Cleft palate, retrognatism, imperforate anus, right uterus bicornis, right ureterocele, pyelocaliceal dilatation, radial ray abnormality, syndactylies and vertebral abnormality	Meckel	
11	E	16	Acrania, medium and lower coelosomy and angular vertebral column	46, XX*	Inencephaly, vertebrocostal dysostosis, exomphalos, colic misalignment and caudal dysgenesis, imperforate anus, renal and uterine agenesis	Possible recurrence	

A, aspiration; *E*, evacuation; *TOP*, termination of pregnancy.

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SUPPLEMENTARY TABLE 3

Fetopathological examination modified genetic counseling in TOP for anterior wall abnormality

Case	Route	Term	Data of the ultrasonographic examination	Karyotype pre or post* TOP	Data of the fetopathological examination complementing the ultrasonographic data	Genetic counseling	Actions to be taken for next pregnancy
12	E	13	Major coelosomy	46, XX*	Short umbilical cord syndrome with thumb hypoplasia, radial hypoplasia, oligosyndactyly	Short umbilical cord syndrome and radial abnormality	

E, evacuation; *TOP*, termination of pregnancy.

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SUPPLEMENTARY TABLE 4

Fetopathological examination modified genetic counseling in the TOP for cephalic pole abnormalities

Case	Route	Term	Data of the ultrasonographic examination	Pre or post* karyotype TOP	Data of the fetopathological examination complementing the ultrasonographic data	Genetic counseling	CAT for next pregnancy
13	E	15	Exencephaly	46, XX*	Anencephalia, cervicodorsal dysostosis, posterior cleft palate, digestive duplication, mitral valve calcification	Possible recurrence	
14	E	16	Exencephaly	46, XY*	Isolated exencephaly, without uronephrological abnormality	No link with anterior pregnancy	
15	A	13	Exencephaly	46, XY	Exencephaly, APSO, single umbilical artery and meconium calcification	Possible recurrence	Cardiac ultrasonography
16	E	15	Iniencephaly	46, XX*	Iniencephaly, raschischisis, spondylocostal dysplasia	Possible recurrence	
17	E	14	Dilatation of ventricle 4, history of Joubert	46, XX*	Dilatation of V4, vermis, midline, dysgenic cranial nerves and dysgenic olivary nuclei	Joubert syndrome AR	
18	A	14	Occipital encephalocele for 1 twin, nuchal translucency 3,6mm	46, XY*	Encephalocele and microphtalmy	Possible recurrence	
19	E	15	Myelomeningocele	46, XY*	Papillary coloboma, hemivertebras, imperforate anus, wrongly differenciated external genital organs	Teratogen	

A, aspiration; *CAT*, computerized axial tomography ; *E*, evacuation; *TOP*, termination of pregnancy.

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SUPPLEMENTARY TABLE 5

Fetopathological examination modified genetic counseling in TOP for hygroma

Case	Route	Term	Data of the ultrasonographic examination	Karyotype pre or post* TOP	Data of the fetopathological examination complementing the ultrasonographic data	Genetic counseling	Actions to be taken for next pregnancy
20	A	13	Hygroma at 5 mm and anasarca	46, XY*	Hepatic calcifications, adrenal cytomegalies, alignment of heart valves	Heart disease	Cardiac ultrasonography
21	E	14	Hygroma at 6 mm	46, XX	Müllerian agenesis, wrongly segmented vertebral column, hypoplasia of left heart	MURCS association	Oriented ultrasonography
22	E	15	Cystic hygroma	46, XY	Hygroma and aortic bicuspidy with elongation of the aortic isthmus	Heart disease	Cardiac ultrasonography

A, aspiration; *E*, evacuation; *MURCS*, Müllerian-renal-cervicothoracic somite abnormalities; *TOP*, termination of pregnancy.

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