Transabdominal versus transcervical and transvaginal multifetal pregnancy reduction: International collaborative experience of more than one thousand cases

Mark I. Evans, MD,[a] Marc Dommergues, MD,[b] Ilan Timor-Tritsch, MD,[c] Ivan E. Zador, PhD,[a] Ronald J. Wapner, MD,[d] Lauren Lynch, MD,[a] Yves Dumez, MD,[b] James D. Goldberg, MD,[f] Kypros H. Nicolaides, MD,[g] Mark Paul Johnson, MD,[a] Mitchell S. Golbus, MD,[f] Pierre Boulot, MD,[h] Alain J. Aknin, MD,[i] Ana Monteagudo, MD,[c] and Richard L. Berkowitz, MD[a]

Detroit, Michigan, Paris and Montpellier, France, New York, New York, Philadelphia, Pennsylvania, San Francisco, California, and London, United Kingdom

OBJECTIVES: Two major approaches for multifetal pregnancy reduction have been developed over the past several years: transabdominal potassium chloride by injection and pelvic procedures by either transcervical aspiration or transvaginal potassium chloride injection or by an automated spring-loaded puncture device. The purpose of this study was to create the largest database from among the world's largest centers to assess possible differences in efficacy and complication rates by transabdominal or transcervical or multifetal pregnancy reduction.
STUDY DESIGN: Data on over 1000 completed pregnancies that underwent multifetal pregnancy reduction by both methods from major centers with among the highest worldwide experience were combined. Transabdominal cases were divided temporally (1986 through 1991 and 1991 through 1993).
RESULTS: Transabdominal multifetal pregnancy reduction was successfully performed on 846 patients and transcervical or transvaginal on 238 patients. Transcervical or transvaginal reduction is performed earlier and starts and finishes with fewer embryos. In 12.6% of cases transcervical or transvaginal reduction left a singleton as opposed to 4.4% for transabdominal reduction. Pregnancy losses (up to 24 weeks) were observed in 13.1% of transcervical or transvaginal cases and in 16.2% of transabdominal cases early in the series and 8.8% of late transabdominal cases. Transcervical or transvaginal reduction may be safer very early in gestation and transabdominal safer later in the first trimester. Premature deliveries were comparable, with only about 5% delivered between 25 and 28 weeks. The smaller starting numbers for transcervical and transvaginal reduction may explain a slightly higher term delivery rate. The transabdominal route tends to reduce the fundal embryos and the transcervical and transvaginal the lower ones. The significance of this is not clear.
CONCLUSIONS: (1) Multifetal pregnancy reduction by either method is a relatively safe and efficient method for improving outcome in multifetal pregnancies. (2) More than 84% are delivered at >33 weeks. (3) The experience and preference of the operator are probably the key determinants for an individual patient. (4) An inverse relationship of starting and finishing number to loss rates and gestational age at delivery suggests that there still is a cost of iatrogenic multifetal pregnancies, even if multifetal pregnancy reduction can be successfully performed. (Am J Obstet Gynecol 1994;170:902-9.)

Key words: Transabdominal, transcervical, transvaginal multifetal pregnancy reduction; prematurity; fetal loss

From the Center for Fetal Diagnosis and Therapy, Departments of Obstetrics and Gynecology, Molecular Biology, and Genetics, Hutzel Hospital/Wayne State University School of Medicine,[a] the Department of Obstetrics and Gynecology, Maternite Port Royal,[b] the Department of Obstetrics and Gynecology, Columbia University Medical School,[c] the Department of Obstetrics and Gynecology, Jefferson Medical College,[d] the Department of Obstetrics and Gynecology, Mt. Sinai Medical School,[e] the Department of Obstetrics and Gynecology, University of California, San Francisco,[f] the Department of Obstetrics and Gynecology, Harris Birthwright Centre, Kings College,[g] the Department of Obstetrics and Gynecology, Hospital de Montpellier,[h] and the Department of Obstetrics and Gynecology, Clinique Michel Bizot-Paris.[i]

Presented at the Fortieth Annual Meeting of the Society for Gynecologic Investigation, Toronto, Ontario, Canada, March 31–April 3, 1993.
Received for publication April 28, 1993; revised October 1, 1993; accepted October 15, 1993.
Reprint requests: Mark I. Evans, MD, Director, Division of Reproductive Genetics, Director, Center for Fetal Diagnosis and Therapy, Hutzel Hospital/Wayne State University, 4707 St. Antoine Boulevard, Detroit, MI 48201.

0002-9378/94 $3.00 + 0 6/1/52274

Over the past 10 years the use of powerful fertility drugs and assisted reproductive techniques have allowed thousands of couples to have their own children.[1] However, there has been a concomitant substantial rise in the numbers of multifetal pregnancies.[2-4] Techniques of multifetal pregnancy reduction have been published over the past several years. Collaborative outcome data have established, to at least an initial degree of satisfaction, the relative safety of multifetal pregnancy reduction certainly compared with the known high morbidity and mortality of attempting to carry multifetal pregnancies, certainly at quadruplets or more, and arguably at triplets.[5-15] The original, published technique of transcervical suction aspiration[5-8] was abandoned in the mid-1980s because of an initial high complication rate and was replaced, at several centers, by transabdominal injection of potassium chloride under ultrasonographic guidance. More recently a few centers with extensive transvaginal ultrasonography experience or experience with in vitro fertilization have revived transvaginal aspiration and also developed a transvaginal approach with an automated, spring-loaded puncture device for potassium chloride injection and mechanical disruption of the embryo.[16] We present here the largest collaborative series of first trimester multifetal pregnancy reduction procedures, comparing outcomes for cases performed transabdominally versus those performed transcervically and transvaginally, collectively referred to here as transvaginally, and to assess with increasing experience our technical progress over the years.

Material and methods

A total of 1074 consecutive patients undergoing multifetal pregnancy reduction with completed pregnancies between 1986 and 1993, were analyzed from several centers, including Wayne State University, Detroit, Maternite Port Royale, Paris, Mt. Sinai, Jefferson, New York, University of California, San Francisco, Columbia University, New York, Clinique Michel Bizot, Paris, Hospital de Montpellier, Montpellier, and Kings College, London. In nearly all cases of triplets or more, the pregnancies were the result of infertility treatments. Procedures were divided into two groups: (1) those performed by transabdominal needle injection of potassium chloride into the fetal thorax and (2) those performed either by transcervical aspiration or transvaginal needle injection of potassium chloride into the fetal thorax and the mechanical disruption of the fetus. These pelvic procedures have mostly been performed during 1991 through 1993. The data for these two pelvic procedures were comparable and combined. Recorded data included the starting and finishing numbers, gestational age at procedure, gestational age at delivery or pregnancy loss, obstetric complications, and congenital malformations.

Results

A total of 1074 consecutive, completed cases are reported here, including 846 transabdominal procedures by potassium chloride injection and 238 transcervical or transvaginal procedures (Table I). About 1% of cases required two procedures to reach the desired goal, mostly in the early years of the series. The distribution of cases by starting number showed proportionately more lower starting numbers, particularly two to one performed transvaginally (transabdominal 4.4%, transcervical/transvaginal 12.6%) (Table II). Overall, the starting and particularly the finishing numbers were higher transabdominally, as was the gestational age at the procedure (Table III).

The pregnancy loss rate (≤ 24 weeks) was slightly higher in the transabdominal group than in the transcervical group and the transvaginal group, but this difference did not reach statistical significance (χ^2 not significant (Table IV). When analyzed by finishing numbers, the loss rates for reduction to singletons were generally higher than for that to twins for all starting numbers (Table V). Within the transabdominal group the pregnancy loss rate was influenced by starting and finishing numbers, and there was a learning curve. We then divided the transabdominal data into two temporal groups. The first was from 1986 through early 1991 (when we put together our first series) and the late cases from then through early 1993. The total loss rate was 13.1% for transvaginal cases, and for the transabdominal cases in the early years the rate was 16.2%, dropping to 8.8% for the later group, showing a very steep learning curve for the safety of the procedure. There are too few transcervical/transvaginal cases to assess a learning curve yet. Adjusted for gestational age at procedure, there were more abdominal losses early and vaginal losses later (Table VI).

One of the principal reasons for performing multifetal pregnancy reduction is the prevention of prematurity. For transabdominal cases 5.2% of patients were delivered between 25 and 28 weeks, 9.9% between 29 and 32 weeks, 39.7% between 33 and 36 weeks, and 45.2% at ≥ 37 weeks. The transvaginal cases were comparable (Fig. 1). Division of transabdominal cases by time series shows a further drop of very premature deliveries from 7.8% to 3.1% (Fig. 2). Overall, for both methods about 84% of all pregnancies reached at least 33 weeks. The gestational age at delivery was also analyzed as a function of the starting and finishing numbers. For both transabdominal and transvaginal

Table I. Distribution of cases

	Starting No.			
	9		*8*	
	Transabdominal	*Transcervical-transvaginal*	*Transabdominal*	*Transcervical-transvaginal*
Triplets	0	0	1	0
Twins	1	0	2	0
Singletons	0	0	0	0
TOTAL	1	0	3	0

Transabdominal 846. Transcervical and transvaginal 238.

Table I—Cont'd

Starting No.					
4		*3*		*2*	
Transabdominal	*Transcervical-transvaginal*	*Transabdominal*	*Transcervical-transvaginal*	*Transabdominal*	*Transcervical-transvaginal*
19	1	–	–	–	–
313	56	301	73	–	–
19	8	40	30	37	30
351	65	341	104	37	30

Table II. Proportion of cases by methods

	Transabdominal		*Transcervical-transvaginal*	
	No.	*%*	*No.*	*%*
≥6	35	4.1	12	5.1
5	82	9.7	27	11.4
4	351	41.5	64	26.9
3	341	40.3	104	43.7
2	37	4.4	30	12.6
TOTAL	846		238	

cases there was an inverse trend of the starting and finishing numbers and the gestational age at delivery, showing that there is still a price to be paid for higher order multifetal pregnancies even if reduction can be performed successfully. However, when finishing number was adjusted, gestational age was independent from starting number.

Congenital malformations were seen in about 1% of all patients—a rate slightly less than background expectations, which may reflect underreporting of delivering physicians around the world and also the fact that, because there is an ultrasonographic search for structural abnormalities before multifetal pregnancy reduction, there may be a selective tendency to reduce those embryos that on the basis of size or nuchal membranes may be at higher risk of having a congenital malformation. Preeclampsia was reported in 1% of patients.

Comment

Over the years multifetal pregnancy reduction has emerged as a surgical response to iatrogenically created multifetal pregnancies. A relatively few centers worldwide have been responsible for the development and application of the procedure. The compilation of data from these centers allows for a much more accurate and sophisticated analysis than would be possible individually. Our data suggest that multifetal pregnancy reduction has improved considerably over time, with decreasing loss rates and decreasing incidence of early premature deliveries. The fact remains, however, that the

Starting No.					
7		*6*		*5*	
Transabdominal	*Transcervical-transvaginal*	*Transabdominal*	*Transcervical-transvaginal*	*Transabdominal*	*Transcervical-transvaginal*
2	0	7	2	9	2
5	3	16	6	71	24
0	0	1	1	2	1
7	3	24	9	82	27

Table III. Transabdominal and transcervical or transvaginal multifetal pregnancy reduction

	No.	*Starting No.*	*Finishing No.*	*Gestational age at procedure (wk)*
Transabdominal	846	3.7 ± 1.0	2.0 ± 0.5	11.3 ± 1.9
Transcervical-transvaginal	238	3.5 ± 1.1	1.7 ± 0.5	9.2 ± 1.8
Significance		$p < 0.01$	$p < 0.00001$	$p < 0.00002$

infertility community must still be vigilant in the use of fertility drugs and assisted reproductive techniques because there is still a higher loss rate and diminished gestational age at delivery for higher-order multifetal pregnancies.

Overall assessment of perinatal morbidity and mortality suggest a fetal loss rate of approximately 16% up to 24 weeks by both methods. Comparison with data on the outcome of well-documented early gestations suggests a roughly comparable fetal loss rate.[1] Loss rates increased with both starting and finishing numbers. There were no outcome correlates within the 8- to 12-week procedure time frame, but there seemed to be a trend for more abdominal losses early and vaginal losses later.

A clear choice of which technique to use is not forthcoming from our data. The slightly higher loss rates transvaginally are confounded by the earlier gestational age at which transcervical/transvaginal cases were performed but countermanded by the lower starting numbers, which should reduce loss rates. Also in the transcervical/transvaginal group three losses of second twins are reported, which were monochorionic twins at the outset and the loss of the second twin was predicted. The further influence of reduction down to singletons is also an unclear contributor to the equation. As such, the best clinical answer seems to be for experienced physicians to use the approach with which they feel most comfortable. The likely result will be that perinatal and genetics-trained physicians will tend to use the transabdominal approach and in vitro fertilization physicians the transvaginal approach. We cannot answer the question about whether reducing fundal or very low implications is better.

The temporal data show a significant reduction in losses and prematurity rates consistent with increasing experience and ultrasonographic visualization. These data support the safety and efficacy of multifetal pregnancy reduction as the centers have moved up the "learning curve." Analysis of our collaborative centers' first 464 cases performed transabdominally showed notably higher loss rate with greater loss rate variation by starting number. Each center has individually noted decreased loss rates with increased experience. It will be interesting to speculate on whether a drop in transcervical/transvaginal losses will accompany increasing numbers of cases by this approach.

The higher loss rate of reducing the singletons by both methods may suggest that the number of needle insertions and the quantity of nonviable tissue may be more important than the number of fetuses remaining. If prevention of prematurity is best achieved when a single embryo is left, this can be obtained only at the cost of a small but significant increase of pregnancy loss rates. However, the singleton data are confounded by a likely selection bias, because many such cases were performed because of special concern about the ability of the mother to carry twins. Thus their high-risk status makes conclusions about the relatively safety of singletons versus twins impossible to ascertain. Most of the authors still routinely suggest that the optimum stopping number is twins, except in circumstances such as poor prior outcome in a twin pregnancy or reason to believe that twins would be significantly compromised in a particular case.

Only 5.2% of women with transabdominal multifetal pregnancy reduction and 5.8% with transcervical/transvaginal with vaiable pregnancies were delivered at ≤28

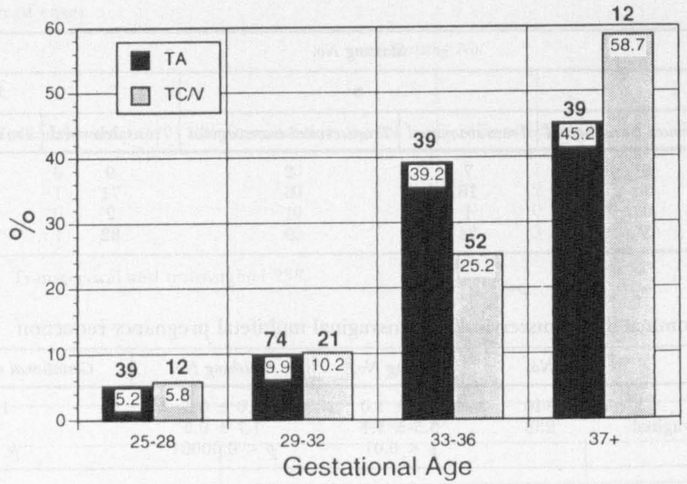

Fig. 1. Histogram detailing gestational age at delivery of viable pregnancies by multifetal pregnancy reduction. Actual number of cases are shown on top of each box and percentage within each box. *TA,* Transabdominal; *TC/V,* transcervical or transvaginal.

Table IV. Early and late losses by method and starting numbers

	Starting No.			
	2		*3*	
	Transabdominal	*Transcervical-transvaginal*	*Transabdominal*	*Transcervical-transvaginal*
<4 wk				
No.	2	4	12	6
%	5.4	13.3	3.5	5.8
All ≤24 wk				
No.	4	5	26	13
%	10.8	16.7	7.6	12.5
Viable				
No.	33	25	315	91
%	89.2	73.3	92.4	87.5
TOTAL	37	30	341	104

Table IV—Cont'd

Starting No.			
6		*≥7*	
Transabdominal	*Transcervical-transvaginal*	*Transabdominal*	*Transcervical-transvaginal*
3	1	1	0
12.5	11.1	9.1	0
12	1	5	1
50	11.1	45.5	33.3
12	10	6	2
50	90.9	54.5	66.7
24	9	11	3

weeks, and about another 10% were delivered between 29 and 32 weeks. Reasons for preterm deliveries were almost exclusively fetal (e.g., preterm labor or premature rupture of membranes). The larger the starting and finishing numbers, the earlier the ultimate delivery. The fact that about 84% were delivered at ≥33 weeks represents a marked improvement on expected outcomes for the neonates who otherwise would have been part of larger multifetal pregnancies.

The incidence of obstetric complications, such as

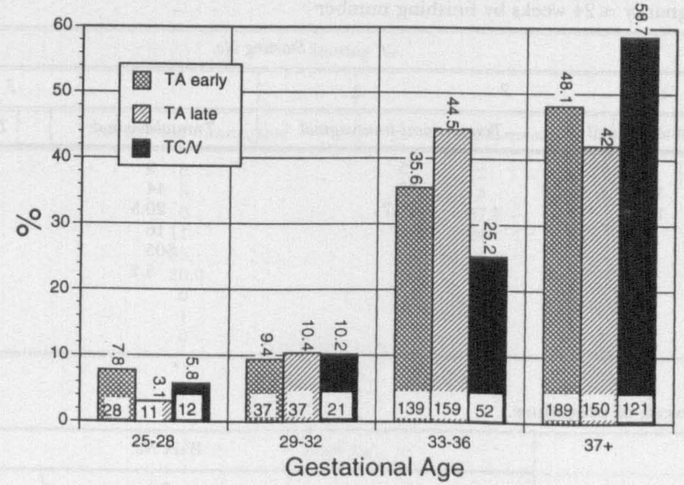

Fig. 2. Time series analysis showing improvement in rate of early prematurity of transabdominal *(TA)* multifetal pregnancy reduction performed in early series (1986 through 1991) versus late series (1991 through 1993). Actual sample sizes are shown inside box and percentages on top. *TC/V,* Transcervical or transvaginal.

Starting No.			
4		*5*	
Transabdominal	*Transcervical-transvaginal*	*Transabdominal*	*Transcervical-transvaginal*
8	4	7	1
2.3	6.2	8.5	3.7
41	10	18	1
11.7	15.4	22.0	3.7
310	55	64	26
88.3	84.6	78.0	96.3
351	65	82	27

premature rupture of membranes, preeclampsia, intrauterine growth retardation, and other maternal and obstetric complications, did not appear to be significantly different from that reported for naturally spontaneously conceived twins (some data not shown).[3, 13, 15] The incidence of preeclampsia (1%) was far lower than that expected for multifetal pregnancies, sugesting another less obvious benefit of multifetal pregnancy reduction. There have also been questions about the psychologic adaptation of patients after multifetal pregnancy reduction. Schreiner-Engel et al.[17] have reported adequate psychologic adjustment of patients who have undergone multifetal pregnancy reduction and found that the vast majority of patients have coped well, given the circumstances. The incidence of congenital anomalies was also about 1%, which is lower than that expected, especially with twins.[14] Both complications and anomalies can be explained either by incomplete ascertainment, because these patients were delivered in large numbers of centers worldwide, or by the fact that there is some choice of which fetuses get reduced. All participants in this survey would choose to reduce a fetus that was noticeably smaller, appeared abnormal, or had oligohydramnios. It is therefore possible that to some degree fetuses who would ultimately have abnormalities might be those more likely to be reduced.

Overall, the combined data from the centers represented in this report suggest that the mortality (and the morbidity) of multifetal pregnancies—certainly at four or more and likely at three—can be reduced by multifetal pregnancy reduction. Several years of experience have now increased both the confidence of the physicians performing the procedures and the patients' perception of its relative safety. However, particularly as fetal numbers increased, outcomes were less optimal (i.e., although in most cases acceptable outcomes can be

Table V. Loss of pregnancy ≤24 weeks by finishing number

	Starting No.					
	2		*3*		*4*	
	Transabdominal	*Transcervical-transvaginal*	*Transabdominal*	*Transcervical-transvaginal*	*Transabdominal*	*Transcervical-transvaginal*
Singleton	4	5	9	4	4	0
Total	37	30	44	30	11	8
Percent	10.8	16.7	20.5	13.3	36.4	0
Twins			16	9	36	11
Total			305	74	313	55
Percent			5.2	12.2	11.5	20.0
Triplets					2	0
Total					19	1
Percent					10.5	0

	Starting No.	
	≥5	
	Transabdominal	*Transcervical-transvaginal*
Singleton	2	0
Total	3	2
Percent	67.7	0
Twins	24	3
Total	94	33
Percent	25.5	9.1
Triplets	7	0
Total	19	4
Percent	36.8	0

Table VI. Losses by week of procedure

	Week No.					
	6		*7*		*8*	
	Transabdominal	*Transcervical-transvaginal*	*Transabdominal*	*Transcervical-transvaginal*	*Transabdominal*	*Transcervical-transvaginal*
≤2 wk						
No.	0	1	0	3	1	1
%	–	20	–	11.1	8.3	2.1
≤4 wk						
No.	0	1	1	3	1	1
%	–	20	16.7	11.1	8.3	2.1
≤24 wk						
No.	1	1	1	3	3	3
%	16.7	20	16.7	11.7	21.4	6.3
≥25 wk (No.)	5	4	5	24	11	46

	Week No.					
	9		*10*		*11*	
	Transabdominal	*Transcervical-transvaginal*	*Transabdominal*	*Transcervical-transvaginal*	*Transabdominal*	*Transcervical-transvaginal*
≤2 wk						
No.	0	3	4	3	5	1
%	–	5.2	3.1	6.0	1.6	6.7
≤4 wk						
No.	0	3	7	4	8	1
%	–	5.2	5.2	8.0	2.5	6.7
≤24 wk						
No.	0	9	24	10	39	2
%	0	13.8	16.0	17.9	11.3	12.5
≥25 wk (No.)	24	56	126	46	306	14

Table VI—Cont'd

	Week No.					
	12		*13*		*14*	
	Transabdominal	*Transcervical-transvaginal*	*Transabdominal*	*Transcervical-transvaginal*	*Transabdominal*	*Transcervical-transvaginal*
≤2 wk						
No.	7	2	1	0	2	0
%	3.3	12.5	2.2	–	14.3	–
≤4 wk						
No.	8	2	3	0	2	1
%	3.8	12.5	6.7	–	14.3	–
≤24 wk						
No.	29	2	7	1	2	1
%	12.5	12.5	14.3	50.0	14.3	100
≥25 wk (No.)	203	14	42	1	12	0

achieved even starting with high fetal numbers, there is still a "price to be paid" in increased fetal loss rates and increased risk of prematurity). The point remains very clearly that cavalier infertility treatment does have deleterious effects even if multifetal pregnancy reduction can be performed by trained physicians. Although most infertility specialists appear to be extremely cautious in the use of reproductive medicines and techniques, we are very distressed that a few physicians have become extremely aggressive[18] with assisted reproductive techniques and view multifetal pregnancy reduction as merely an adjunct of such therapies without significant medical or ethical consequences. The data presented here show conclusively that there is still a price to be paid by their patients for such attitudes.

REFERENCES

1. Medical Research International. Society for Assisted Reproductive Technology—American Fertility Society. In vitro fertilization—embryo transfer (IVF-ET) in the United States: 1990 results from the IVF-ET Registry. Fertil Steril 1992;57:15-24.
2. Collins MS, Bleyl JA. Seventy-one quadruplet pregnancies: management and outcome. Am J Obstet Gynecol 1990; 162:1384-92.
3. Luke B, Keith LG. The contribution of singletons, twins and triplets to low birthweight, infant mortality and handicap in the United States. J Reprod Med 1994 [in press].
4. Evans MI, Fletcher JC. Multifetal pregnancy reduction. In: Reece EA, Mahoney MJ, Petrie PH, eds. Medicine of the fetus and mother. Philadelphia: JB Lippincott, 1992:1336-45.
5. Martene-Duplan J, Aknin AJ, Alamowitch R. Aspiration embryonnaire partielle au cours de grossesses multiples. Contracept Fertil Sexual 1983;11:745-8.
6. Dumez Y, Oury JF. Method for first trimester selective abortion in multiple pregnancy. Contrib Gynecol Obstet 1986;15:50.
7. Salat-Baroux J, Aknin J, Antoine JM, Alamowitch R. The management of multiple pregnancies after induction for superovulation. Hum Reprod 1988;3:399-401.
8. Dommergues M, Nisand I, Mandelbrot L, Isfer E, Radunovic N, Dumez Y. Embryo reduction in multifetal pregnancies following infertility therapy: obstetrical risks and perinatal benefits are related to operative strategy. Fertil Steril 1991;55:805-11.
9. Evans MI, Fletcher JC, Zador IE, Newton BW, Quigg MH, Struyk CD. Selective first trimester termination in octuplet and quadruplet pregnancies clinical and ethical issues. Obstet Gynecol 1988;71:289-96.
10. Berkowitz RL, Lynch L, Chitkara U, et al. Selective reduction of multiple pregnancies in the first trimester. N Engl J Med 1988;318:1043.
11. Wapner RJ, Davis GH, Johnson A. Selective reduction of multifetal pregnancies. Lancet 1990;335:90-3.
12. Evans MI, May M, Drugan A, Fletcher JC, Johnson MP, Sokol RJ. Selective termination: clinical experience and residual risks. Am J Obstet Gynecol 1990;162:1568-75.
13. Lynch L, Berkowitz RL, Chitkara U, Alvarez M. First trimester transabdominal multiple pregnancy reduction: a report of 85 cases. Obstet Gynecol 1990;75:735-8.
14. Tabsh KM. Transabdominal multifetal pregnancy reduction: report of 40 cases. Obstet Gynecol 1990;75:739-41.
15. Evans MI, Dommergues M, Wapner RJ, et al. Efficacy of transabdominal multifetal pregnancy reduction: collaborative experience among the world's largest centers. Obstet Gynecol 1993;82:61-6.
16. Timor-Tritsch IE, Peisner DB, Monteagudo A, Lercner JP, Sharma S. Multifetal pregnancy reduction by transvaginal puncture: evaluation of the technique used in 134 cases. Am J Obstet Gynecol 1993;168:799-804.
17. Schreiner-Engel D, Walther V, Mindes J, Lynch L, Berkowitz RL. First trimester multifetal pregnancy reduction: acute and persistent psychological reactions. Obstet Gynecol 1994 [In press].
18. Avers JWT, Petersen EP, Knight L, Peterson S. Incorporation of transvaginal embryo reduction (TVER) with an aggressive IVF/GIFT/ZIFT program to optimize pregnancy outcome. Fertil Steril 1991;56:5173.