Intrauterine blood transfusion : indications, risks, quality control and long-term outcome

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Chapter 4

Quality control for intravascular intrauterine transfusion using cumulative sum (CUSUM) analysis for the monitoring of individual performance

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Abstract

Introduction: Intravascular intrauterine transfusion (IUT) is an effective and relatively safe method for the treatment of fetal anemia. Although implemented in centers all over the world in the 1980s, the length and strength of the learning curve for this procedure has never been studied. Cumulative sum (CUSUM) analysis has been increasingly used as a graphical and statistical tool for quality control and learning curve assessment in clinical medicine. We aimed to test the feasibility of CUSUM analysis for quality control in fetal therapy by using this method to monitor individual performance of IUT in the learning phase and over the long term.

Methods: IUTs performed in the Dutch referral center for fetal therapy from 1987 to 2009 were retrospectively classified as successful or failed. Failed was defined as no net transfusion or the occurrence of life-threatening procedure-related complications. The CUSUM statistical method was used to estimate individual learning curves and to monitor long-term performance. Four operators who each performed at least 200 procedures were included.

Results: Individual CUSUM graphs were easily assessed. Both operators pioneering IUT in the late 1980s had long learning phases. The 2 operators learning IUT in later years in an experienced team performed acceptably from the start and reached a level of competence after 34 and 49 procedures.

Discussion: CUSUM analysis is a feasible method for quality control in fetal therapy. In an experienced setting, individual competence may be reached after 30 to 50 IUTs. Our data suggest that operators need at least 10 procedures per year to keep a level of competence.

Introduction

Intravascular intrauterine blood transfusion (IUT) is considered a relatively safe and effective method to correct life-threatening fetal anemia due to maternal red blood cell alloimmunization. This technique was introduced in the early 1980s [1, 2] and is nowadays routinely applied in expert centers for fetal therapy all over the world [3, 4] Without correction for individual learning processes and team experience, IUT is associated with a procedure-related fetal loss of 1.6% per procedure [5] .

Several studies have analyzed the length and strength of a learning phase for various non-invasive and invasive procedures during pregnancy [6–11]. Generally, successful performance is not only influenced by the operator's skills and experience but also by factors related to the patient as well as to team performance [6, 7]. New operators are able to perform diagnostic ultrasound-guided procedures without increase in complications if supervised by a limited number of experienced operators in a high-volume centralized care setting [7, 8]. However, despite more than 20 years of worldwide experience with intrauterine blood transfusion, there are no reliable data on the aspects of the learning curve for this procedure.

Cumulative sum (CUSUM) analysis was designed to control the performance of industrial processes. This statistical and graphical method of quality control shows changes in performance. Apart from quality control, CUSUM analysis may estimate the number of procedures needed to achieve a predetermined level of acceptable performance. The CUSUM method is increasingly used in medicine for quality control monitoring and more recently for learning curve assessment [12]. CUSUM analysis can be applied for all procedures with a binary outcome, such as success or failure, but requires predefined levels of acceptable and unacceptable performance. The primary aim of our study was to test the feasibility of CUSUM analysis for quality control in fetal medicine. CUSUM was used to estimate learning curves for IUT and as a method to monitor individual performance after the learning process has been completed. Data derived from our study may serve as a guidance for the monitoring of individual training and long-term performance of intrauterine transfusions.

Material and Methods

Operators and Procedures Since 1965, the Department of Obstetrics of the Leiden University Medical Center has served as the single referral center in the Netherlands for the management of pregnancies complicated by maternal red cell alloimmunization. Intrauterine blood transfusion was initially performed intraperitoneally [13]. After high resolution ultrasound became available in obstetrics, intravascular transfusion techniques replaced the intraperitoneal method in Leiden in March 1987. Our methods for the management of alloimmunization in pregnancy and technical aspects of intravascular fetal transfusion have been described previously [3]. From 1987 onward, data on all intravascular intrauterine transfusions performed in our center were prospectively collected in a database. All intravascular intrauterine transfusions performed from March 1987 up to January 2009 were retrospectively classified as failed or successful. Criteria for classifying a procedure as failed were: – true failures: failure to administer a net volume of blood into the fetal circulation; – occurrence of life-threatening procedure-related complications: emergency cesarean section within 24 h and perinatal death within 7 days after the procedure. Classification of complications into procedure- or not procedure- related was performed by 2 independent observers who followed criteria previously described [5]. Total failure rates were calculated for consecutive years and for the total series in order to define acceptable and unacceptable failure rates as input for the CUSUM analysis. All operators who performed at least 200 procedures and had no prior experience with IUT were considered eligible for this study. Individual prior experience with other ultrasound-guided invasive procedures, such as intraperitoneal intrauterine transfusion, chorionic villus sampling and amniocentesis was assessed. Individual experience with IUT was assessed by describing the number of procedures performed in consecutive years and the corresponding failure and success rates. Factors that may influence the outcome of IUT such as gestational age, presence of fetal hydrops, severity of fetal anemia and use of fetal paralysis at the procedure were compared for all procedures performed by each operator. Duration of the procedure was not taken into account, as this variable mainly depends on transfusion volume and thus on gestational age.

CUSUM Analysis

To apply a CUSUM analysis, 4 obligatory parameters have to be defined: the predefined acceptable (p_0) and unacceptable failure rates (p_1) for the procedure concerned, the type I (α) error (false-positive error, would lead to the conclusion that performance is unacceptable when it is not) and the type II (β) error (false-negative error, would lead to the conclusion that performance is acceptable when it is in fact unacceptable). The following equations are used to calculate the intermediate values of CUSUM analysis (value ln is the natural logarithm or log e):

$a = \ln [(1 – \beta)/ \alpha]$
$b = \ln [(1 – \alpha)/ \beta]$
$P = \ln (p_1 /p_0)$
$Q = \ln [(1 – p_0)/(1 – p_1)]$
$s = Q/(P + Q)$
$h_0 = b/(P + Q)$
$h_1 = a/(P + Q)$.

The results of a CUSUM analysis are generally visualized in a CUSUM graph, representing performance during a number of consecutive procedures. In the graph, procedure numbers are plotted on the x-axis and the corresponding actual CUSUM values on the y-axis. The actual CUSUM value is obtained by cumulatively subtracting a value ‘s’ for each successful procedure and adding ‘1 – s’ for each failed procedure. Hence, success is rewarded by a certain downward slope whereas failure is punished by a much more pronounced upward slope in the graph. The horizontal limit lines or boundaries in CUSUM graphs are defined by the factor ‘h‘ that determines the spacing between unacceptable (h_0) and acceptable boundaries (h_1). Based on the statistical background of the CUSUM method, crossing 2 boundaries in the downward direction indicates competent performance, whereas competence declines after crossing 2 boundaries upwards. After a second boundary crossing one may retrospectively conclude, from a clinical point of view, that performance has already been acceptable from the first boundary crossing downwards or unacceptable from the first crossing upwards. Crossing boundaries in upward direction is normal in a learning situation.

In our study, acceptable and unacceptable failure rates for intrauterine transfusion were based on the overall performance in the cohort and set at, respectively, 4% and 10% (data in the ‘Results’ section). In CUSUM analysis, a convenient choice of 0.1 for both type I and II errors is common. With different values for type I and II errors, the plot may become unclear and unreadable due to inequality of h_0 and h_1 values. Therefore, type I and II (α and β) errors were both set at 0.1, according to most studies using a CUSUM technique. After calculation, the s value was 0.066 and the distance between acceptable (h_1) and unacceptable (h_0) limit lines was identical (2.24). Thus, for each failure, the actual CUSUM value will increase with 0.934 (1–s) and for each success it will decrease with 0.066 (s).

Additional Statistical Analysis

Data were collected and analyzed in a database using SPSS version 16.0 (SPSS, Inc., Chicago, Ill., USA). The homo- or heterogeneity of variables of performed procedures per operator was listed for comparison. The X^2 test was used for comparing the variables hydrops fetalis and the use of fetal paralysis. Comparison of the variables hemoglobin and gestational age at procedure was evaluated with Student's t test. In tables, $p < 0.05$ was considered to indicate statistical significance.

Results

Operators and Procedures

In the study period, a total of 1,390 intravascular IUTs were performed by 8 operators. The overall success rate of intravascular fetal transfusion in this 21-years period was 96% (1,330/1,390). Sixty failures (4%) consisted of 29 'true failures' (inability to administer net intravascular transfused blood) and 31 complications (13 emergency caesarean sections and 18 perinatal deaths). Annual failure rates were especially high in the first 4 years (18, 16, 13, and 12% respectively), and gradually declined from about 10% to 0–2% in later years. The overall failure rate of 4% and the highest annual failure rate of 10% in the years after 1990 were used as input in the CUSUM analysis to set the acceptable and unacceptable failure limits.

Four operators met the criteria for entering the study. These 4 operators performed 85% of all procedures (1,184/1,390). Operators 1 and 2 had performed transfusions since the implementation of intravascular IUT in the Netherlands in 1987, whereas operators 3 and 4 started in 1993 and 1996 respectively. All operators were randomly assigned for the procedures. In table 1, the number of procedures performed, individual success rates and prior experience with ultrasound-guided invasive procedures are summarized. Operator 1 was the only person having performed intraperitoneal intrauterine transfusions. All operators had varying experience with ultrasound- guided diagnostic procedures.

Table 1. *Operator's success and experience.*

Operator	Period	Procedures *(n)*	Success rate *(%)*	Annual procedures *(mean number)*	Prior experience[a] *(years)*
Operator 1	1987- 2008	298	90.9	14	>5
Operator 2	1987- 2009	319	95.6	15	0.5
Operator 3	1993- 2009	339	97.6	22	2.5
Operator 4	1996- 2009	228	98.7	19	4

[a]Defined as experience with other ultrasound-guided invasive procedures (intraperitoneal transfusion, chorionic villus sampling and amniocentesis)

The number of annually performed procedures (both successful and failed) of all operators are shown in figure 1. Operator 1 performed fewer procedures in later years, due to increasing administrative obligations. In the last 8 years of the study, operator 1 performed a mean of 4 procedures per year (SD 3). Operator 2, temporarily performed fewer procedures in 1997 and 1998 for health reasons, but kept performing a mean of 15 procedures annually (SD 3) in later years. Operators 3 and 4 had a steady annual mean performance of 22 (SD 8) and 19 (SD 8) procedures respectively. Operator 1 and 2 had the highest total failure rates of 9.1 and 4.4%, the majority of failures occurring in the late 1980s and early 1990s. Operators 3 and 4 had total failure rates of 2.4 and 1.3%, respectively. Characteristics of procedures performed per operator are summarized in table 2. Operator 1 performed procedures at an earlier mean gestational age and treated more severely anemic and hydropic fetuses than the other operators. In addition, fetal paralysis was less frequently applied at procedures performed by operator 1.

Figure 1. *Number of performed procedures per operator per year. White = successful; black = failed.*

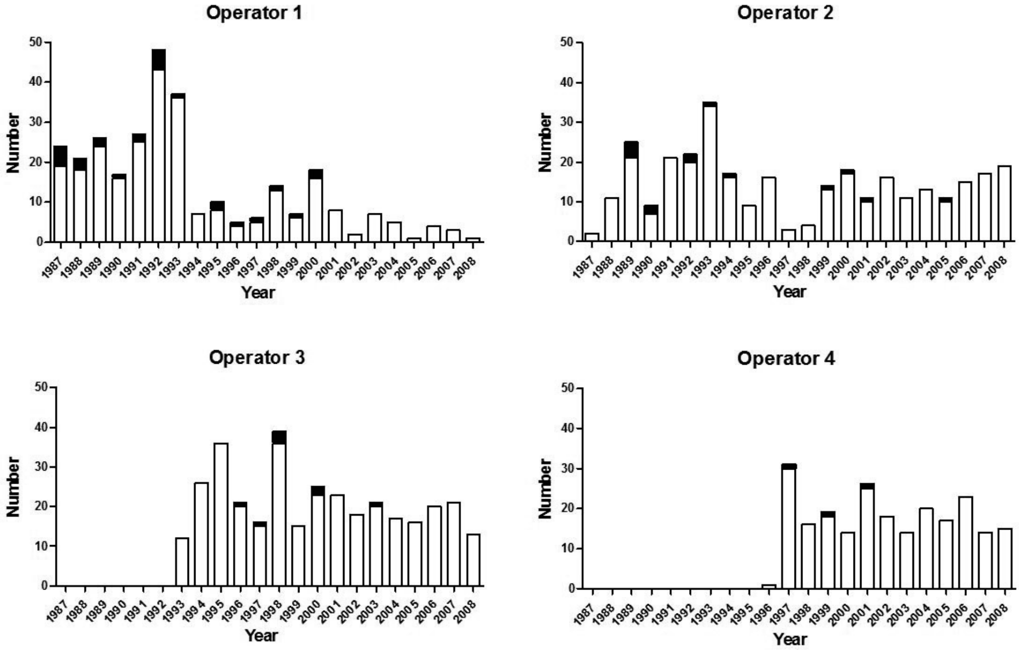


Table 2. *Characteristics of intrauterine transfusions performed per operator.*

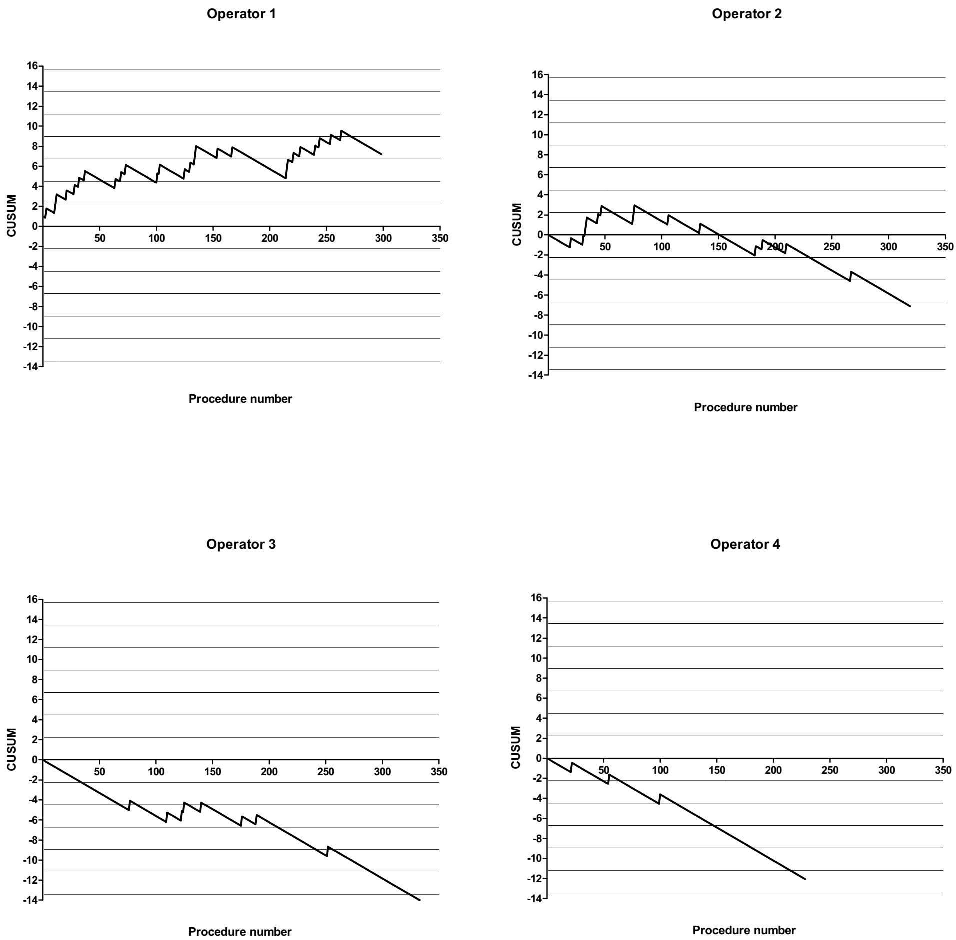
	Operator 1 *(n=298)*	p	**Operator 2** *(n=319)*	p	**Operator 3** *(n=339)*	p	**Operator 4** *(n=228)*
Gestational age at IUT[a], *weeks*	28 (4)	0.003[b]	30 (4)	NS[b]	30 (4)	NS[b]	30 (4)
Hemoglobin at IUT[a], *g/dL*	3.9 (1.3)	0.046[b]	4.1 (1.3)	NS[b]	4.2 (1.3)	NS[b]	4.2 (1.4)
Fetal hydrops at IUT, *n (%)*	66 (22)	0.042[c]	48 (15)	NS[c]	56 (17)	NS[c]	44 (19)
Fetal paralysis[d] *n (%)*	193 (74)	<0,001[c]	262 (87)	NS[c]	298 (91)	NS[c]	212 (93)

NS, no significance; [a]Data in mean ± SD; [b]Calculated with Independent Sample Test/ Student t Test; [c]Calculated with Chi Square Test; [d]Corrected for missing data (38, 17 and 11 procedures for operator 1, 2 and 3).

CUSUM Analysis

Operator 1 started in 1987 as a pioneer in an inexperienced team and had the longest learning phase (fig. 2). The CUSUM graph of this operator shows a distinct downward slope after 185 procedures performed, resulting in a first downward boundary crossing. However, competence was not confirmed by a second boundary crossing. Operator 2, starting supervised by operator 1 in 1987, had a shorter learning curve. Performance of this operator improved after procedure 57 indicated by a downward boundary intersection in the CUSUM graph. However, an upward boundary crossing at procedure 76 obstructed the achievement of a level of competence. At procedure 87 a new downward crossing is followed by a second one at procedure 151, indicating acceptable performance and thus completing of the initial learning phase after 87 procedures. Operators 3 and 4 started respectively 8 and 10 years after the implementation of intravascular IUT in our center. They required 34 and 50 procedures respectively to achieve a level of competence. The downward trend in both CUSUM graphs from the first procedure indicates acceptable performance from the start.

Figure 2. *Individual CUSUM graphs representing CUSUM analysis. The consecutive number of performed procedures on the x-axis is plotted against the actual CUSUM value on the y-axis. The CUSUM value is the cumulative sum of increments (0.934, with each failure) and decrements (0.066 for each success). The horizontal lines represent (un)acceptable boundary lines (spacing 2.24).*



Discussion

In this study, we aimed to test the feasibility of CUSUM analysis as a statistical method for monitoring individual competence in invasive fetal therapy. CUSUM was used to estimate learning curves and to monitor long term performance of 4 operators, who altogether performed nearly 1,200 intrauterine blood transfusions in a time span of 22 years in the single Dutch referral center for fetal therapy. We experienced that CUSUM may be easily accomplished and results in clarifying graphs as a visual guidance of individual performance. Several statistical methods are available for individual learning curve assessment and quality control [12, 14–16]. These methods are all based on sequential monitoring of performance over a period of time, generally using quality limits. The simplest method of charting is the cumulative failure graph, in which each failure results in a 45° slope and each success in a horizontal line. Although this method is applicable for small data sets, changes of performance over the long-term may not be easily identified [17].

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Most CUSUM techniques are based on predefined levels of success or failure. Consecutive successes and failures are immediately accounted for by either subtracting or adding a statistically determined factor. The boundaries, or quality limits, in CUSUM graphs, are derived from the Sequential Probability Ratio Test by Wald [18]. CUSUM control charts were originally designed to monitor the quality of industrial productions. After World War II, CUSUM was used as a quality control test for munitions production. The statistical background of the CUSUM technique was first described in detail by Page in 1954 [19]. Subsequently, a major increase of CUSUM implementation was seen, especially in clinical chemistrylaboratories [20]. In clinical medicine the need for quality control arose [21, 22], but only in the early 1990s several medical studies used CUSUM analysis to monitor operators' performance and to describe learning curves [23, 24]. Nowadays, CUSUM analysis is increasingly used for various clinical procedures [25–28]. Risk-adjusted CUSUM has the advantage to take into account variations in pre-procedure or pre-operative risks [29], but these must be identifiable and clearly defined. In this first CUSUM study in fetal therapy, we used a standard nonrisk- adjusted method, as described by Bolsin et al. [17].

The 2 operators pioneering this new technique in an inexperienced setting had the longest learning phase. Operator 1 seemed to reach acceptable performance after 185 procedures, but failed to reach a level of competence. Operator 2 performed acceptably from procedure 87 onward and was declared competent at procedure 151. Operators 3 and 4, learning IUT under supervision and in an experienced setting, both performed acceptably from the start and reached competent performance after 34 and 50 procedures respectively. As our study is restricted to 4 operators from a single center, it seems improper to conclude that our learning curves are representative of those performing IUT in other fetal medicine units. Future prospective multicenter CUSUM studies may further elucidate all aspects of gaining and guarding competence for intrauterine transfusion. CUSUM may well be applied for prospective monitoring of the individual learning process for IUT. In this respect, we suggest that supervision by an experienced operator is no longer necessary after reaching a competence level in the CUSUM graph.

The longer learning processes of the first 2 operators may be explained in the first place by the lack of any experience with this new technique in the early years. This accounts not only for those actually performing the procedure, but also for other team members being responsible for the ultrasound-guidance and the preparation of the blood product. Additionally, ultrasound equipment improved remarkably during the study period, including the introduction of Doppler, facilitating IUT technique. In the 1980s, intravascular fetal transfusion had just been implemented in centers all over the world and competence had to be gained by those performing the procedures. Operators 3 and 4 started performing IUT in an experienced setting under supervision, allowing them to start off with the easier procedures. Operator 2 had some supervision from the first operator, who had prior experience with intraperitoneal fetal transfusion.

A second explanation for the higher incidence of failed procedures may be the fact that the first operator, performing the majority of the procedures in the late 1980s and early 1990s, treated significantly more hydropic and severely anemic fetuses and performed transfusions at earlier gestational ages than the other operators. In a prior study, we demonstrated that procedure-related complications of IUT more frequently occur at earlier gestational ages [5]. Operators 2, 3 and 4 seem to have benefited in this respect from the earlier identification of pregnancies at risk, resulting from the implementation in the Netherlands in 1998 of a routine red cell antibody screening of all women in the first trimester of pregnancy. In addition, the early diagnosis of fetal anemia was gradually facilitated in the past decades by the use of MCA Doppler, allowing the start of intrauterine treatment before the development of fetal hydrops [30].

In order to avoid procedure-related complications, the use of fetal paralysis is recommended and transamniotic cord puncture as well as arterial puncture should best be avoided [5]. After completing the study on this subject, the recommendations on transfusion technique were implemented in our fetal therapy team. In the early years, fetal paralysis was not routinely applied. Operator 1 used no fetal paralysis in about one fourth of the procedures performed. This may additionally have contributed to the higher occurrence of failed procedures.

We chose to define failed procedures both as ‘true failures’, generally followed by a second attempt, and as serious life-threatening procedure-related complications. We decided to include all serious procedure-related complications as failed procedures, as the operator may be held responsible for the occurrence of the problem. Data on acceptable and unacceptable failure rates of IUT are lacking in the literature. Therefore, we had to derive these figures from our own series of 1,390 procedures, which is the largest ever published. As the predefined acceptable and unacceptable failure rates of 4 and 10% were derived from the total cohort, it may be assumed that these limits are too low for operators 3 and 4 and too strict for the first 2 operators, who encountered all the initial problems related to IUT. In future studies using CUSUM, it is essential to reconsider the limits of acceptable and unacceptable performance.

After gaining competence in 1992, 1994 and 1999 respectively, operators 2, 3 and 4 continued to cross boundaries in the downward direction in their CUSUM graphs, indicating preservation of an expert level. These operators all performed at least 10 procedures annually. Instead of a second downward boundary crossing, the CUSUM plot of operator 1 shows an unexpected upward slope after approximately 200 procedures, indicating a deterioration of performance. We hypothesize that the decline in performance of this operator may be related to the relatively low number of procedures performed annually in later years. A similar effect was observed in the CUSUM graph of operator 2 after approximately 170 procedures, showing a temporarily upward slope that may be explained by having performed fewer procedures in the preceding years (1997 and 1998). The fact that operator 1 had no failures during the last 8 years seems to contradict our hypothesis, but may be coincidence, due to the small number of procedures annually performed. From these results, we hypothesize that individual competence in intravascular intrauterine transfusion may best be warranted if at least 10 procedures are being performed annually. In this respect, we agree with Urbaniak et al. [31], who empirically recommended 10–15 intrauterine transfusions per year to maintain competence.

All operators in our study had experience with needling under ultrasound-guidance. Although our data do not allow conclusions on the exact benefit of prior experience on the learning process for IUT, we do agree with others suggesting that experience with less invasive procedures is indispensable before starting to perform more invasive and therapeutic ultrasound-guided procedures in fetal medicine [6–8] .

In conclusion, we demonstrated that CUSUM analysis is a feasible method for monitoring individual learning processes for and long-term performance of intravascular IUT. CUSUM methods may well be used for quality control, not only in fetal therapy, but for all invasive procedures in clinical medicine. The learning phase for IUT in an experienced setting is short, allowing acceptable performance from the start. In this respect, centralization of knowledge and skills is of great importance in order to create an optimal climate for trainees starting to learn this technique. Our study indicates that the number of IUTs needed to be supervised by a senior operator may vary from around 30 to 50 procedures. In addition, experienced operators may best maintain their level of competence by performing at least 10 intrauterine transfusions annually. Future prospective multicenter CUSUM studies are needed to validate these numbers.

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References

1. Daffos F, Capella-Pavlovsky M, Forestier F. A new procedure for fetal blood sampling in utero: preliminary results of fifty-three cases. Am J Obstet Gynecol 1983;146:985–987.
2. Bang J, Bock JE, Trolle D. Ultrasound-guided fetal intravenous transfusion for severe rhesus haemolytic disease. Br Med J (Clin Res Ed) 1982;284:373–374.
3. Van Kamp IL, Klumper FJ, Meerman RH, Oepkes D, Scherjon SA, Kanhai HH. Treatment of fetal anemia due to red-cell alloimmunization with intrauterine transfusions in the Netherlands 1988–1999. Acta Obstet Gynecol Scand 2004;83:731–737.
4. Moise KJ Jr. Management of rhesus alloimmunization in pregnancy. Obstet Gynecol 2008;112:164–176.
5. Van Kamp IL, Klumper FJ, Oepkes D, Meerman RH, Scherjon SA, Vandenbussche FP, et al. Complications of intrauterine intravascular transfusion for fetal anemia due to maternal red cell alloimmunization. Am J Obstet Gynecol 2005;192:171–177.
6. Silver RK, MacGregor SN, Sholl JS, Hobart ED, Waldee JK. An evaluation of the chorionic villus sampling learning curve. Am J Obstet Gynecol 1990;163:917–922.
7. Wijnberger LD, van der Schouw YT, Christiaens GC. Learning in medicine: chorionic villus sampling. Prenat Diagn 2000;20:241– 246.
8. Perry KG Jr, Hess LW, Roberts WE, Allbert JR, Floyd RC, McCaul JF et al. Cordocentesis (funipuncture) by maternal-fetal fellows: the learning curve. Fetal Diagn Ther 1991;6:87– 92.
9. Maiz N, Kagan KO, Milovanovic E, Celik E, Nicolaides KH. Learning curve for Doppler assessment of ductus venosus flow at 11 + 0 to 13 + 6 weeks’ gestation. Ultrasound Obstet Gynecol 2008;31:503–506.
10. Cicero S, Dezerega V, Andrade E, Scheier M, Nicolaides KH. Learning curve for sonographic examination of the fetal nasal bone at 11–14 weeks. Ultrasound Obstet Gynecol 2003;22:135–137.
11. Nizard J, Duyme M, Ville Y. Teaching ultrasound- guided invasive procedures in fetal medicine: learning curves with and without an electronic guidance system. Ultrasound Obstet Gynecol 2002;19:274–277.
12. Biau DJ, Resche-Rigon M, Godiris-Petit G, Nizard RS, Porcher R. Quality control of surgical and interventional procedures; a review of the CUSUM. Qual Saf Health Care 2007;16:203–207.
13. Bennebroek Gravenhorst J, Kanhai HH, Meerman RH, Ruys JH, Eernisse JG, Stroes TJ, et al. Twenty-two years of intra-uterine intraperitoneal transfusions. Eur J Obstet Gynecol Reprod Biol 1989;33:71–77.

14. Noyez L. Control charts, Cusum techniques and funnel plots: a review of methods for monitoring performance in healthcare. Interact Cardiovasc Thorac Surg 2009;9:494–499.
15. Lane S, Weeks A, Scholefield H, Alfirevic Z. Monitoring obstetricians' performance with statistical process control charts. BJOG 2007;114:614–618.
16. Poloniecki J, Sismanidis C, Bland M, Jones P. Retrospective cohort study of false alarm rates associated with a series of heart operations: the case for hospital mortality monitoring groups. BMJ 2004;328:375.
17. Bolsin S, Colson M. The use of the Cusum Technique in the assessment of trainee competence in new procedures. Int J Qual Health Care 2000;12:433–438.
18. Wald A. Sequential analysis. New York, Wiley, 1947.
19. Page ES. Continuous inspection schemes; in Biometrika, University of Cambridge, 1954, vol 41, pp 100–115.
20. Rowlands RJ, Griffiths K, Kemp KW, Nix AB, Richards G, Wilson DW. Application of Cusum techniques to the routine monitoring of analytical performance in clinical laboratories. Stat Med 1983;2:141–145.
21. Wohl H. The CUSUM plot: its utility in the analysis of clinical data. N Engl J Med 1977;296:1044–1045.
22. Chaput de Saintonge DM, Vere DW. Why don't doctors use CUSUMS? Lancet 1974;1:120–121.
23. Williams SM, Parry BR, Schlup MTM. Quality control: an application of the CUSUM. BMJ 1992;304:1359–1361.
24. Kestin IG. A statistical approach to measuring the competence of anaesthetic trainees at practical procedures. Br J Anaesth 1995;75:805–809.
25. Yap C, Colson ME, Watters DA. Cumulative sum techniques for surgeons: a brief review. ANZ J Surg 2007;77:583–586.
26. Choi DH, Jeong WK, Lim SW, Chung TS, Park JI, Lim SB, et al. Learning curves for laparoscopic sigmoidectomy used to manage curable sigmoid colon cancer: single-institute, three-surgeon experience. Surg Endosc 2009;23:622–628.
27. Claerhout F, Roovers JP, Lewi P, Verguts J, De Ridder D, Deprest J. Implementation of laparoscopic sacrocolpopexy: a single centre's experience. Int Urogynecol J Pelvic Floor Dysfunct 2009;20:1119–1125.
28. Weerasinghe S, Mirghani H, Revel A, Abu- Zidan FM. Cumulative sum (CUSUM) analysis in the assessment of trainee competence in fetal biometry measurement. Ultrasound Obstet Gynecol 2006;28:199–203.

29. Rogers CA, Reeves BC, Caputo M, Ganesh JS, Bonser RS, Angelini GD. Control chart methods for monitoring cardiac surgical performance and their interpretation. J Thorac Cardiovasc Surg 2004;128:811–819.
30. Oepkes D, Brand A, Vandenbussche FP, Meerman RH, Kanhai HH. The use of ultrasonography and Doppler in the prediction of fetal haemolytic anemia: a multivariate analysis. Br J Obstet Gynaecol 1994;101:680–684.
31. Urbaniak SJ, Greiss MA. RhD haemolytic disease of the fetus and newborn. Blood Rev 2000;14:44–61.