

Simultaneous bilateral single-stage combined open reduction and pelvic osteotomy for the treatment of developmental dysplasia of the hip

Abdulmonem Alsiddiky^a, Raheef Alatassi^b, Mahdi M. Alqarni^a and Khalid Bakerman^a

Children older than 18 months with developmental dysplasia of the hip (DDH) for the first time or who do not respond to closed treatment require open reduction with/without acetabuloplasty. We determined whether open reduction and pelvic acetabuloplasty using the Pemberton or Dega technique for both hips simultaneously was well tolerated and offered better outcomes. A total of 140 hips of 70 patients with bilateral DDH were identified. All patients were diagnosed after they started walking. Patients were treated with bilateral single-stage open reduction with acetabuloplasty using the Pemberton or Dega procedure. All patients were prospectively followed up between 2007 and 2018. Results were considered satisfactory if the acetabular index was $<24^\circ$. Hemoglobin levels were evaluated in all patients. At the final follow-up, the results were evaluated radiologically and clinically based on the modified Severin's classification and modified McKay criteria, respectively. The mean age at surgery was 20.3 months (range, 16–24). The mean operative time was 228 minutes. The mean postoperative hemoglobin level was 90.5 g/L (range, 61–122; SD, ± 13.4).

Background

Developmental dysplasia of the hip (DDH) refers to a range of developmental hip disorders. It is a major pediatric orthopedic problem, and is one of the most debated diseases because of its treatment [1]. Management of DDH aims to achieve a stable, concentric, and anatomically reduced femoral head inside the acetabulum without causing avascular necrosis. This can be performed using a closed or open technique. Multiple methods have been described in the literature for the management of DDH; the method used is chosen according to the age of the child and preference of the surgeon [2,3]. As the child becomes older, the closed procedure becomes more difficult and a surgical option becomes more favorable [4,5]. Children older than 18 months who present with DDH for the first time or who do not have a response to closed treatment require open reduction with or without acetabuloplasty and femoral shortening [6]. However, various approved techniques for acetabuloplasty have been designed to treat acetabular dysplasia in DDH. Pemberton [7] described pericapsular pelvic osteotomy for acetabuloplasty in 1965.

The mean differences between the preoperative and postoperative acetabular index values for both hips were 22.36° (SD, $\pm 6.69^\circ$) and 22.64° (SD, $\pm 6.69^\circ$) for the right and left hips, respectively. Open reduction with pelvic acetabuloplasty using the Pemberton or Dega technique simultaneously in both hips was well tolerated, cost-effective, had excellent outcomes, and posed no additional risk to patients with DDH younger than 24 months. *J Pediatr Orthop B XXX:000–000* Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

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In contrast, Dega [8] described supraacetabular semicircular osteotomy in 1958.

DDH is more common in the left hip; however, it shows bilateral involvement in approximately 20% of cases. In bilateral cases, management is more complicated and challenging for the surgeon, patient, as well as parents [9]. A single-stage surgical approach including open reduction and pelvic osteotomy appears to be preferable for treating children diagnosed late with DDH (>18 months) based on the existing literature [5,10,11]. However, studies reporting a simultaneous bilateral single-stage approach to treat DDH are limited and they include small numbers of patients with short-term follow-up periods [12–14].

In this study, we assessed the efficacy of open reduction accompanied with pelvic acetabuloplasty using the Pemberton or Dega technique simultaneously and bilaterally for the treatment of DDH in children younger than 2 years. We measured safety in terms of hip instability and blood loss along with functional, clinical and radiographic outcomes. In addition, the cost-effectiveness and psychosocial impact of the procedure were discussed.

Materials and methods

Patient selection and follow-up

In this study, 140 hips of 70 patients with bilateral DDH diagnosed after they began walking were included. Our inclusion criterion for the study were: children between 18 and 24 months of age, had bilateral, complete hip dislocation and all of them were Tönnis [15] Grade IV. We performed prospective follow-up between 2007 and 2018 at our institution. All patients were treated in the same manner by bilateral single-stage open reduction with acetabuloplasty using the Pemberton or Dega procedure, followed by a hip spica cast performed under general anesthesia during the same surgery. The hip spica cast was later changed to a bilateral broomstick cast, and each was applied for at least 6 weeks. Follow-up visits were required every six weeks during the first 6 months postoperatively. A period of 2 years was considered the minimum follow-up time for inclusion in the study. Children with neuromuscular disorders, previous avascular necrosis (AVN), or paralytic or traumatic dislocations and those who had previously undergone two-stage bilateral or unilateral open reduction were excluded from the study. Notably, preliminary traction was not used in any case. In addition, any patient requiring proximal femoral osteotomy was excluded from the study. During the course of this study, we did not perform staged bilateral open reduction and acetabuloplasty in any case with bilateral DDH. Moreover, no case was converted from bilateral to unilateral open reduction and acetabuloplasty during the same period.

All parents provided written informed consent to use the information of their children in this study. The study was approved by the local research ethics committee at our institution. All children were treated by two orthopedic surgeons. In addition, the same goniometer was used to evaluate the preoperative and postoperative radiographs. These were assessed by two different orthopedic surgeons who were not involved in the care of patients. The acetabular index was used to evaluate the patients preoperatively and postoperatively. Complications such as AVN of the femoral head, lateral subluxation, and redislocation were recorded. Furthermore, both coxa magna and mild epiphyseal changes were considered as AVN. Acetabular development was considered satisfactory when the acetabular index was $<24^\circ$. In addition, hemoglobin levels were evaluated preoperatively and postoperatively in all patients. We assessed the hemoglobin level at 6 and 24 hours after casting (hip spica). If the hemoglobin level was below 8 mg/dl, we indicated the use of blood transfusion. Regarding the range of motion (ROM), we considered the patient to have full ROM if he/she achieved the following motions of the hip: flexion 120° , extension 30° , abduction 45° , internal rotation 35° , and external rotation 45° [16].

All patients were followed up in the pediatric orthopedic clinic at 6, 12, 18, and 22 weeks after surgery. At each

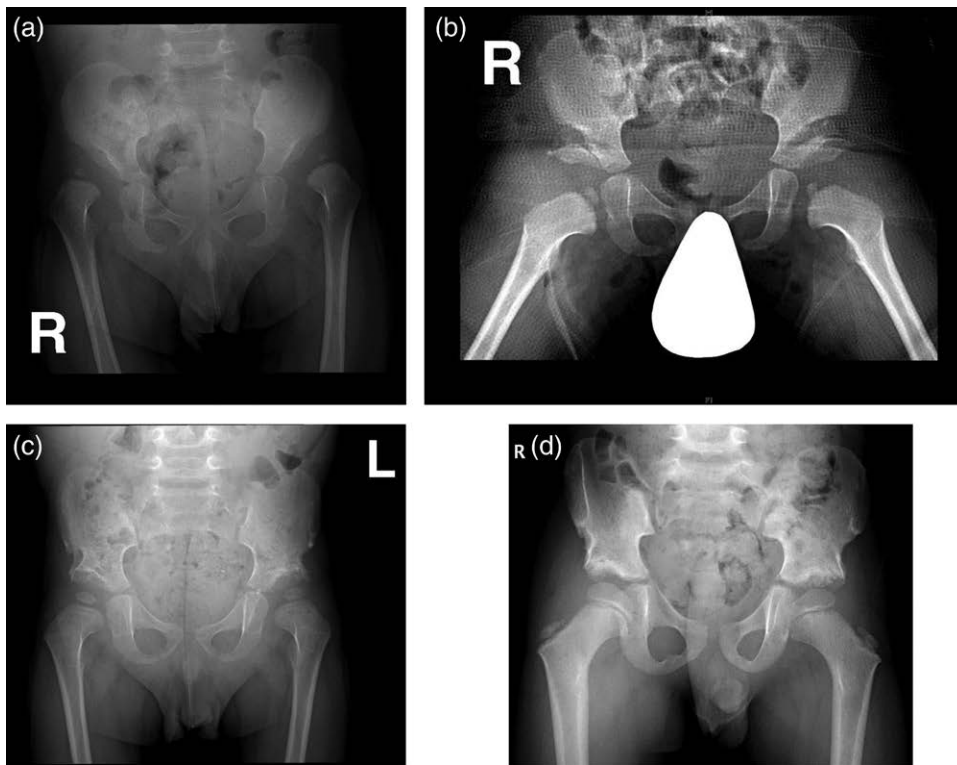
follow-up examination, an anteroposterior radiograph of the pelvis was obtained to assess acetabular development and ensure the efficacy of surgery. We performed radiographic imaging to evaluate the concentricity of the reduction achieved with acetabular index and to check for any complications such as AVN. At 6 weeks, the hip spica cast was changed to the broomstick cast in the clinic. At 12 weeks, complete removal of the cast was performed and gentle ROM with gait training exercises were encouraged for home therapy. At 18 weeks, status of the reduction and osteotomy, ROM and any stiffness were determined. If patients showed any sign of stiffness in either hip, they were sent directly to the physiotherapy department for extensive ROM exercises. At 22 weeks, another assessment of ROM was performed. Following this, patients were followed up every 6 months for three visits; thereafter, they were followed up annually. At the final follow-up, the results were evaluated radiologically by a pelvic radiograph based on the modified Severin's classification [17]. A class I (excellent) result was considered when the hip showed a normal shape. A class II (good) result was considered when the proximal femur, head or neck or both had moderate deformities. Both class I and II results were required to have a center-edge angle of $>19^\circ$. Additionally, at the final follow-up, we assessed all patients' clinical outcomes based on the modified McKay criteria [18]. Anteroposterior and lateral frog leg radiographs of the hip were obtained at each visit, followed by clinical assessment of ROM. Representative radiographs obtained before and 2 years after surgery are shown in Fig. 1.

Operative technique

Surgery consisted of adductor tenotomy, capsulotomy, open reduction, acetabuloplasty, and spica cast application. Briefly, under general anesthesia, we began with patient installation and positioning of both the patient and the c-arm (radiograph). We installed the patient at the lower edge of the table. Our draping protocol is to drape the lower half of the patient completely, starting from the nipples area downward till the feet. In addition, we draped the patient from front and back. We used a 'U' shaped drape to isolate the upper half of the body from the lower half. Moreover, we covered the genital area using a small sterile drape (Fig. 2). We used the c-arm (radiograph) to assist us while performing the acetabuloplasty. After we draped the c-arm, we positioned it at the lower middle edge of the table (at the patient's foot side) in order to allow us to perform the surgery in both hips without losing time to change the c-arm position (Fig. 3).

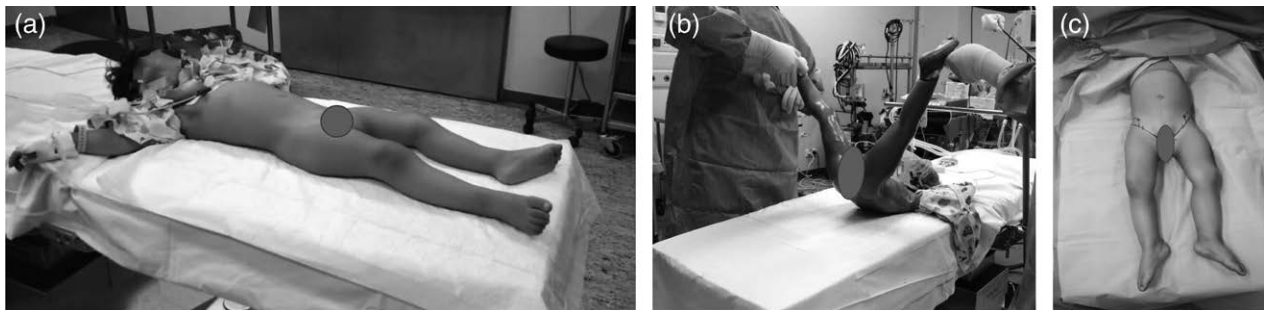
Subsequently, the operation began with percutaneous adductor longus tenotomy after cleaning and draping both hips. An anterior approach to the hip was used, and the direct head of the rectus femoris muscle and iliopsoas tendon were released. The joint capsule was opened to access all obstacles for open reduction of the

Fig. 1



Plain radiographs of the pelvis of one patient obtained during different visits. (a) Anteroposterior (AP) radiograph obtained at the first visit at 18 months of age. It shows bilateral hip dysplasia with dislocation. (b) AP radiograph obtained after simultaneous bilateral open reduction with pelvic osteotomy. (c) AP radiograph obtained at 22 weeks after the surgery. (d) AP radiograph obtained at 28 months after the surgery.

Fig. 2



Details of the preparation steps for patient installation and draping during the operation. (a) We installed the patient at the lower edge of the table. (b) We draped the lower half of the patient completely, both in the front and back. The draping was done from the nipples downward till the feet. (c) A 'U' shaped drape was used to isolate the upper half of the body from the lower half.

hip. The ligamentum teres and pulvinar were excised in all patients, and the transverse ligament was incised. Next, the femoral head was reduced into the hip. A pelvic osteotomy was performed either using the Pemberton or Dega approach. The choice of pelvic osteotomy was made preoperatively, and approaches were alternated with each patient to avoid bias and ensure the efficacy of

both techniques. The same procedure was performed on the other hip, and the stability of both hips was checked. Next, capsulorrhaphy followed by skin closure was performed. Subsequently, patients were immobilized in a hip spica for 6 weeks with the hip positioned at 30° of flexion and abduction. Reduction was confirmed intraoperatively using radiography. All patients received the

Fig. 3

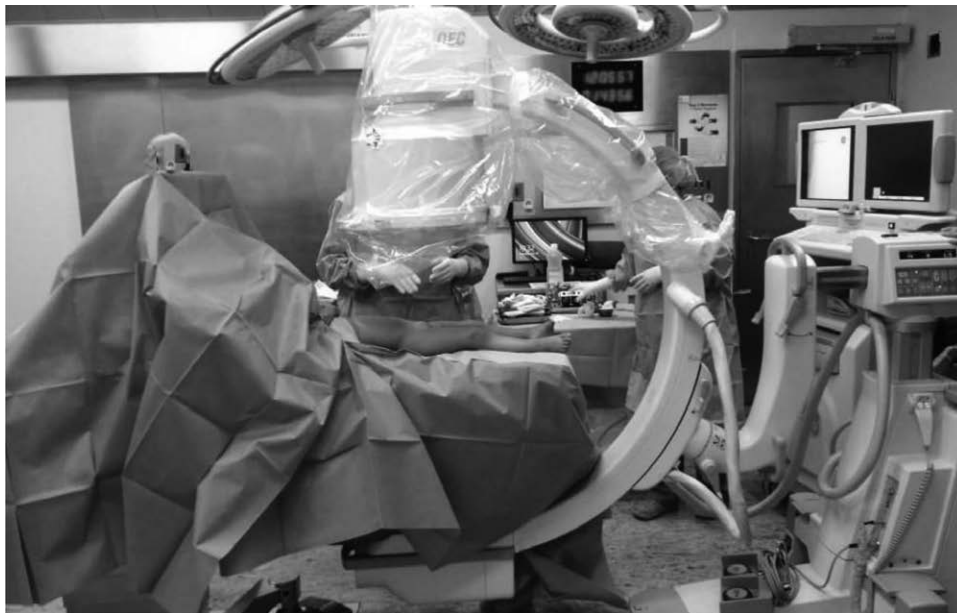


Illustration of the position of the c-arm during the operation. The c-arm was positioned at the middle lower edge of the table (at the patient foot side). The c-arm was draped before starting the operation.

same standard antibiotic therapy (first-generation cephalosporin) preoperatively and postoperatively. All patients were discharged the next day unless a complication occurred.

Statistical analysis

Clinical and operative data collected for the study included age, sex, comorbidities, hemoglobin level, length of stay, and time required for bilateral open reduction and acetabuloplasty (operation time). Specific DDH data were obtained preoperatively and postoperatively at 2 years which included bilateral acetabular index, bilateral ROM, and any occurrence of complications such as AVN, lateral subluxation, or dislocation of the hip. Descriptive and analytical statistical analyses were performed using paired Wilcoxon tests, Student's *t*-tests, and paired *t*-tests. Statistical analyses of the data were performed using SPSS Statistics for Windows, version 23 (SPSS Inc., Chicago, Illinois, USA). Differences were considered significant if $P < 0.05$.

Results

Patient characteristics are shown in Table 1. None of the patients were lost or excluded from the study due to lack of data or missed follow-ups. Independent *t*-tests revealed no significant differences in study outcomes or complications regardless of sex or age at the time of surgery. In addition, there were no differences in the development of AVN, lateral subluxation, or redislocation ($P > 0.05$) regardless of sex or age at the time of surgery.

Table 1 Clinical and operative characteristics of the study patients

Sex (n, %)	Male	8 (11.4)
	Female	62 (88.5)
Mean age at surgery, months (range)	Male	21.4 (17–28)
	Female	24.1 (16–48)
	Total	20.8 (16–48)
Mean operative time, minutes (range) ^a		228 (131–325)
Mean blood loss, ml (range) ^a		80.71 (60–150)
Mean postoperative hemoglobin level, g/L (range)		90.5 (61–122)
Mean blood transfusion (range)		143.2 (100–200)

^aMean operative time including application of the cast.

The mean preoperative acetabular index values for the right and left hips were $43.90^\circ (\pm 4.74^\circ)$ and $44.10^\circ (\pm 4.42^\circ)$, respectively; the mean postoperative acetabular index values for the right and left hips were $21.61^\circ (\pm 4.45^\circ)$ and $21.46^\circ (\pm 4.25^\circ)$, respectively. Paired samples *t*-tests revealed significant differences between preoperative and postoperative acetabular index values for the right and left hips (mean difference, right hip: $22.36^\circ \pm 6.69$ and $P = 0.0001$; mean difference, left hip: $22.64^\circ \pm 6.69$ and $P = 0.0001$).

None of our patients exhibited neurovascular injury, surgical wound infection, or graft displacement. Moreover, no intraoperative or immediate postoperative complications were documented in any of the patients. Three hips (4.2%) of three patients experienced postoperative lateral subluxation with limited ROM, as shown by failure of the cross-leg test. Immediate physiotherapy was

performed in these patients. Lateral subluxation was attributable to early removal of the cast in one patient and required a second procedure with k-wire fixation. Two right hips (2.85%) of two patients developed redislocation, which was associated with limited flexion and internal rotation. Both underwent a second open reduction and capsulorrhaphy procedure. Two hips (2.85%) of two patients developed AVN, which was recorded as a poor outcome. Furthermore, 19 (26.6%) hips in 17 patients required postoperative physiotherapy. The average blood loss during the operation was 80.7 ml. Markedly, all blood transfusions were performed after the surgery. A total of 22 patients (31.4%; mean age, 20.0 months) in this study required transfusions. No patients developed complications due to the transfusions. At the final follow up, both clinical and radiological outcomes were evaluated based on the modified McKay and modified Severin's classifications, respectively. One hundred fifteen (82.1%) of the 140 hips were graded with excellent clinical outcomes. Twenty-one (15%) hips that were stable, painless, without limping or negative Trendelenburg signs, and had a full range of movement on each side, were considered to have good results. Hip function was fair in 2 (1.4 %) hips due to limited ROM. However, 2 (1.4%) hips were graded to have a poor outcome. Besides, 132 (94.2%) hips were classified to have excellent results (class I) and 8 (5.7%) were classified to have good results (class II) based on Severin's classification. The mean center-edge angle was $34.6^{\circ} \pm 3.9$ at the final follow-up.

Discussion

The goals of treatment for DDH are to concentrically reduce the hip, maintain it in a stable position without damaging the blood supply or causing any damage to the

hip, maintain reduction, and create a well remodeled hip [2,4,8–10]. Performing a single surgery that includes open reduction and pelvic osteotomy with or without femoral shortening in children younger than 4 years has been described previously and has shown promising results; however, the technique can be challenging [5,10,11,19–22]. Moreover, few studies have reported performing a single surgery bilaterally and simultaneously [12–14]. The main concerns regarding this procedure are hip stability, blood loss, and long operative time, which make this procedure very difficult to execute and increase the operative risk.

Agus *et al.* [13] compared bilateral simultaneous open reduction and pelvic osteotomy vs. unilateral surgeries to treat DDH in patients above the walking age. After around 50 months of follow-up, they found no significant differences between the two groups in terms of clinical and radiological outcomes. In addition, there was no significant difference in postoperative acetabular index correction between the two groups. Other studies have shown excellent results when performing single-stage open reduction and pelvic osteotomy, either unilaterally or bilaterally in a sequential manner [10,23]. Therefore, we used these groups as controls for our study. A detailed clinical and radiological comparison between unilateral, sequential bilateral, and simultaneous bilateral open reduction and pelvic osteotomy to treat DDH is presented in Table 2.

Salter [24] reported that simultaneous bilateral pelvic osteotomy is contraindicated. He recommended performing each hip osteotomy at least 2 weeks apart because the simultaneous procedure may cause technical errors, which result in the loss of fixation or pelvic instability. However, that article was published in 1961; to the best

Table 2 Comparisons of demographics, as well as preoperative, clinical and radiological outcomes between unilateral, sequential bilateral, and simultaneous bilateral groups that underwent open reduction and pelvic osteotomy to treat developmental dysplasia of the hip

	Simultaneous bilateral group; current study	Unilateral group; Agus <i>et al.</i> [13]	Unilateral group; Baki <i>et al.</i> [10]	Sequential group; Subasi <i>et al.</i> [23]
Number of hips	140	12	32	22
Female, (%)	62 (88.5%)	9 (75%)	21 (65.6%)	–
Hip Tönnis grade, (%)	140 (100%) grade IV	4 (30%) grade III 8 (70%) grade IV	20 (62.5%) grade II 9 (28.1%) grade III 3 (9.3%) grade IV	3 (13.6 %) grade III 19 (86.3%) grade IV
Acetabular index (mean)				
Preoperative	Right 43.90°; left 44.10°	38.8°	40.1°	36.9°
Postoperative	Right 21.61°; left 21.46°	28.6°	8.9°	20.2°
Correction	Right 22.36°; left: 22.64°	10.2°	31.2°	16.7°
Center-edge angle (Mean)	34.6°	–	35.5°	25.5°
Severin classification				They used the modified score system of Trevor to assess both clinical and radiological outcomes
I (Excellent)	132 (94.2%) (I)	–	29 (90.6%) (I)	
II (Good)	8 (5.7%) (II)	–	3 (9.4%) (II)	
III (Fair)	–	–	–	
IV (Poor)	–	–	–	
Modified McKay grade				
I (Excellent)	115 (82.1%) (I)	–	30 (93.7 %) (I)	13 hips (59.1%) (I)
II (Good)	21 (15 %) (II)	–	2 (6.3 %) (II)	3 (13.6%) (II)
III (Fair)	2 (1.4 %) (III)	–	–	6 (27.3%) (III)
IV (Poor)	2 (1.4 %) (IV)	–	–	–

of our knowledge, no other study has reported this as a contraindication. Pemberton and Dega pelvic osteotomies are considered incomplete osteotomies because the pelvic ring remains unaffected. Using these techniques, we hypothesized that bilateral simultaneous pelvic osteotomy was theoretically possible [7,8]. In the present study, we confirmed our hypothesis as only a few cases showed hip instability or loss of fixation. In addition, 136 (97.1%) hips were considered to have satisfactory clinical results, including both excellent and good outcomes. Furthermore, we confirmed that the bilateral simultaneous pelvic osteotomy can be performed using both the Pemberton and Dega surgical techniques.

Performing simultaneous single-stage bilateral open reduction with pelvic osteotomy is considered extensive and more invasive than the unilateral procedure because the longer operative time increases the exposure to anesthesia and increases the risk for blood transfusions. In this study, 31% patients required transfusions; however, we found no postoperative complications associated with this. Two previous studies reported the use of combined bilateral pelvic osteotomy [13,14]. In those studies, all patients required blood transfusions and compared to our study, a higher mean volume of blood was required. Furthermore, the moderate increase in the requirement for blood transfusions in this study was not associated with any increase in morbidity or mortality. However, patients who required transfusion in our study did mostly due to postoperative oozing. Fortunately, no major complications occurred operatively or postoperatively. We recommend considering usage of tranexamic acid or small bowl cell-savers in cases where bleeding is extensive during the operation to minimize the rate of blood transfusion. Nevertheless, the use of tranexamic acid or small bowl cell-savers in pelvic osteotomy in that age group lacks evidence and further studies are needed to validate its use.

Ezirmik and Yildiz [14] reported that the mean duration of anesthesia was 180 minutes in their study; this was significantly lower than that in the sequential group, which had a mean anesthesia duration of 450 minutes. However, they did not report whether this included the time required for cast application. In the present study, the mean total operative time, including open reduction, pelvic osteotomy, and cast application, was 228 minutes, which is not that long, because the procedure was performed by experts. When a nonexpert surgeon performs this procedure, the operative time might be longer. Regardless of who performs the procedure, the operative time is not a significant obstacle to simultaneous bilateral combination surgery.

However, several studies have shown that multiple exposures to anesthesia before the age of 4 years is considered a significant independent risk factor for developing learning disabilities and poor academic performance later in life. In addition, these studies state that single exposure to anesthesia during surgery before the age of

4 years has no association with or any adverse effects on cognitive or behavioral outcomes [25–27]. Schneuer *et al.* [26] concluded in their population-based cohort study that in general, poorer school performance and development at school entry were noticed in children who have been exposed to general anesthesia before the age of 4 years. However, in children who had only been exposed to general anesthesia once in a single hospital admission had reduced risk. In addition, we cannot conclude whether children exposed to a long duration (>120 minutes) of anesthesia in a single exposure have any poorer outcomes [26].

The acetabular index is a radiographic parameter routinely used by pediatric orthopedic surgeons to evaluate hip conditions of younger children with DDH. Additionally, acetabular index values are used to plan the treatment protocol (e.g., the type of pelvic osteotomy) and to measure outcomes. A normal acetabular index value is usually defined as 20° for children 2 years of age (range, 20°–22°) [28,29]. In our study, all patients were between 18 and 24 months of age, with mean preoperative acetabular index values of 44.1° and 43.9° for the left and right hips, respectively. All patients were eligible for both types of pelvic osteotomy. Furthermore, our study showed a remarkable improvement in the acetabular index for both hips after surgery. All patients achieved the primary outcome of acetabular index <24° during the follow-up period.

AVN is one of the worst complications associated with the treatment of DDH because it can result in unavoidable deformities. Multiple theories regarding the cause of AVN have been described. The consensus is that as age increases, the risk of developing AVN postoperatively increases. The mean incidence of AVN after open reduction and pelvic osteotomy ranges from 7 to 22% [12–14,30–32]. In our study, only two out of 140 (2.85%) hips developed AVN, and postoperative physiotherapy was required only in 19 (26.6%) hips of 17 patients for different reasons. Almost all patients who developed complications recovered to full ROM, concentrically reduced hips, and normal walking without limping at the last follow-up examination. Furthermore, none of the patients developed other complications, such as fracture or wound infection. Our results demonstrated a significant improvement in the need for postoperative transfusions compared with other studies that reported single-stage bilateral open reduction and pelvic osteotomy (Table 3) [13,14].

Performing simultaneous bilateral pelvic osteotomy has important benefits. This procedure reduced hospitalization time by half, which probably might lead to significant social and economic impacts on the family and child, decreased morbidity associated with hospitalization, and avoiding the need of a second surgery, which has additional risks such as anesthesia exposure. Additionally, the

Table 3 Differences in demographics, outcomes, and complications among similar studies that performed a single-stage bilateral pelvic osteotomy procedure

Variables/studies	Current study	Agus <i>et al.</i> [13]	Ezirmik <i>et al.</i> [14]
Single-stage bilateral pelvic osteotomy (patient number)	70	12	63
Female (%)	62 (88.5%)	10 (83.1%)	57 (90.4%)
Mean age at surgery (months)	20.8	31.0	24.0
Tönnis grade	Type IV: 140 (100%)	Type III: 6 (25%) Type IV: 18 (75%)	Type I: 1 (0.8%) Type II: 85 (67.5%) Type III: 30 (23.8%) Type IV: 10 (7.9%)
Follow-up (months)	48.7	54.8	71.4
AVN, <i>n</i> (%)	2 (2.85%)	5 (20.8%)	5 (7.9)
Transfusion, <i>n</i> (%)	22 (31.4%)	12 (100%)	–
Mean transfusion volume, (ml)	143.2	170	200

AVN, avascular necrosis.

total cost of patient management was reduced. Patients were admitted once and underwent a single surgery, which required fewer follow-up visits. Two sequential surgeries require separate, and therefore additional, follow-up visits. Moreover, the risk of hip stiffness was reduced because the period of immobilization in the cast was minimized. Performing two sequential surgeries requires at least 3 months of immobilization for each hip. In this study, immobilization was reduced to 6 weeks.

Our study revealed that simultaneous bilateral open reduction and pelvic osteotomy for children with bilateral DDH who are younger than 2 years achieved excellent outcomes with very limited and treatable complications. Additionally, the costs of admission and hospitalization with all the necessary equipment were decreased when a single surgery was performed. Furthermore, one surgery is preferable for children and their parents. To the best of our knowledge, this study showed significant clinical outcomes using the largest cohort for comparison. Most studies stated that their major limitations were limited patient numbers and short-term follow-up [12–14]. Therefore, we believe that there were no contraindications to perform this procedure, especially when an expert surgeon considered all precautions.

Limitations

This study had some limitations. First, there was no control group for comparison with the study population. However, we compared our results with those of other studies that had a control group, comprising of patients treated with either, a unilateral procedure or staged bilateral procedures. Therefore, this study could not directly compare simultaneous and sequential surgery in the study population. Nevertheless, we reported the results of our experience with simultaneous surgery, which is not well reported in the literature. Second, no specific or accurate score was used to evaluate the psychosocial impact of performing such surgery. Further studies that focus on the psychosocial impact and include accurate measurements of such an impact are necessary to validate our results.

Conclusion

Performing open reduction accompanied by pelvic acetabuloplasty using the Pemberton or Dega technique simultaneously in both hips is well tolerated and has no contraindications for the treatment of DDH in children who are younger than 2 years. Furthermore, this procedure had better outcomes in terms of hip stiffness, cost-effectiveness, and possibly psychosocial impact.

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A.A. reviewed the final version of the manuscript. R.A. performed the literature review, statistical analysis, and wrote the manuscript. M.M.A. performed the data collection and contributed to writing the manuscript. K.B. contributed to writing the manuscript.

Conflicts of interest

There are no conflicts of interest.

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