Does the type of anesthesia influence the outcome after modular proximal mega prosthesis for bone metastases of the femur?

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Abstract : *Background :* Proximal femoral reconstruction with modular mega prosthesis after large oncologic resection is a long-lasting painful procedure associated with prolonged hospital stay and significant blood loss. We evaluated the influence of regional anesthesia on intraoperative and postoperative complications as well as length of hospital stay (LOS).

Materials and Methods : We performed a retrospective study comparing three regimens of anesthesia on intraoperative and postoperative complications after proximal femoral reconstruction with mega prosthesis. Seventy-two patients were included. 26 of whom had general anesthesia (GA) alone (group 1), 21 had GA combined to lumbar epidural anesthesia (group 2) and 25 had GA combined to lumbar plexus block (group 3). Surgical procedures were similar and carried out by the same surgeon.

Results : Demographic characteristics were equivalent between 3 groups, except for age and ASA score. Intraoperative variables were similar between groups except for intraoperative blood loss ($p = 0.007$), blood transfusion ($p = 0.004$) and opioids consumption ($p = 0.01$). Pulmonary infections were more frequent in group 1 compared to other groups ($p = 0.036$). Postoperative hypoventilations were less frequent in group 3 (p = 0.022). There were no difference for local complications, luxation and LOS. Type of anesthesia was found to be an independent predictive factor for intraoperative blood loss (p = 0.014), postoperative respiratory hypoventilation (p = 0.014) and respiratory infection (p = 0.011).

Conclusion : Loco regional anesthesia, especially lumbar plexus block, may reduce blood loss, transfusion and postoperative complications after modular mega prosthesis for proximal femoral malignant lesions.

Keywords: lumbar plexus block ; epidural ; anesthesia ; mega prosthesis ; metastatic ; femur.

Introduction

After the liver and the lungs, the bone is a major site of solid tumor metastases such as breast, lung, prostatic and renal carcinomas. Thirty to sixty percent of bone metastases are mainly located in the spine and long bones such as the femur**. (1, 2).

Moreover, primary bone tumors, such as Ewing's sarcoma, chondrosarcoma and osteosarcoma are also generally located at this level (2).

Femoral bone tumors may cause significant morbidity including pain, pathological fractures, joint instability, nerve or vascular lesions, impairment of ambulation and reduced functional independence (3)**. Previous research showed that pathological fractures are observed in 9 to 29 % of patients with long bone metastases, and a high proportion of these require surgical intervention to relieve pain and restore function (4, 5).

Metastatic femoral bone lesions are generally treated by open internal fixation with or without bone cement (6, 7). This procedure becomes more difficult for extensive lesions involving the proximal femur because of the high stress on this weight bearing area. Therefore, many orthopedists favor mega prosthetic reconstruction after tumor resection (8, 9). However, this long lasting procedure is more invasive and associated with longer hospital stay and greater blood loss (10).

With the developments of anesthetic modalities and availabilities, regional anesthetic techniques, such lumbar plexus block or epidural anesthesia, are increasingly used in combination with general anesthesia, mainly in elderly and comorbid patients. Regional anesthesia reduces the use of postoperative systemic opioids and thus reduce or avoid their adverse effects (11, 12, 13)**.

In a recent systematic review, lumbar plexus block demonstrated a reduction in postoperative pain scores. When intrathecal opioids increased pruritus, lumbar plexus block reduced nausea and pruritus (14).

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Over its role in the management of perioperative pain, regional anesthesia also appears to have an effect on intraoperative blood loss (15, 16, 17).

Among regional techniques, peripheral nerve blocks are gaining popularity because they provide effective analgesia and anesthesia with potentially fewer complications and side effects than central blocks (18).

The three main nerves of the lumbar plexus contribute to the innervation of the lower limb. Blockade of these nerves, combined with the sciatic blockade, can produce complete blockade of the lower limb (19, 20).

A combination of lumbar plexus block with general anesthesia may provide better analgesia with fewer complications compared to general anesthesia alone (21).

The purposes of our retrospective study was to assess the additional benefit of regional anesthesia combined to general anesthesia on intraoperative as well as postoperative complications for proximal modular mega prosthesis after extensive resection of femoral bone malignancies.

Materials and Methods

After the approval of the Ethics Medical Committee (Institut Jules Bordet, Heger Bordet street 1, Brussels. Intern number: CE2561. Dr Lossignol 14-07-2016) we reviewed medical records and anesthesia protocols of 72 patients with metastatic disease or primitive oncologic disease of the proximal femur treated with modular mega prosthetic reconstruction from January 1999 to June 2016 at Jules Bordet Institute.

The procedure was performed by the same experienced surgeon. The following patient charac- teristics were collected from medical records: age, gender, weight, height, body mass index (BMI), American Society of Anesthesiologists (ASA) score, past medical history: cardiovascular risk factors including diabetes and smoking, chronic medication use including anticoagulants and non- steroidal anti-inflammatory drugs (NSAID), and alcohol use. Preoperative and postoperative blood tests *i.a*. hematocrit (Hct) and hemoglobin (Hb) as well as the tumor characteristics and their definitive histopathological examinations were noted. Intra- operative data were also collected regarding peri- operative information. From anesthesia protocols (manuscript or electronic, according to their availability), we collected : length of surgery and anesthesia, type of anesthesia with drugs and their dosages, type and quantity of administered fluids, hemodynamic data and intraoperative blood loss, transfusion and diuresis. Postoperative data were collected from ICU postsurgical files. Postoperative blood loss, morphine and piritramide consumption for first 24 postoperative hours, and postoperative respiratory complications, cardiac complications, infectious complications and pros- thesis complications for the duration of the stay were noted.

To collect respiratory complications, we analyze radiological protocols realized by our radiologists. Pulmonary infections were reported when the radiological images were correlated with a positive microbiology.

Three groups were constituted based on the type of anesthesia: general anesthesia alone (GA), general anesthesia combined to epidural blockade (EPI) and general anesthesia combined to lumbar plexus block (LPB).

Characteristics of patients are presented in tables 1 and 2 according to the type of anesthesia.

General anesthesia with intubation was total intravenous according to the standards used in our institute. Patients were invasively monitored by an arterial line, a central venous line and a core temperature measurement. Noninvasive monitoring included cardiac monitoring by electrocardiogram (ECG), oximeter, capnography and bispectral index. The patient's body temperature was kept constant by a heating blanket.

To perform the lumbar plexus block, the patient was placed in the lateral decubitus position (Sim's position) with operating side above. Anatomical location was performed at the level of L3 vertebra. A posterior paravertebral approach was used. Needle was perpendicularly inserted to the skin with the nerve stimulator initially delivering a current of 2.5 mA (1.5 mA, 2 Hz, 0.1-0.3 ms). Local twitches of the paravertebral muscles were observed at a depth of a couple centimeters. The needle was further advanced, until twitches of the quadriceps muscle were observed (with a mean depth of 6 to 10 cm). The current intensity was then reduced to produce stimulation between 0.45 and 0.5 mA. Particular attention was given to lower limb motor response, which could indicate misplacement in dura mater. When catheter was in place, a bolus of 20 ml of ropivacaine 0.5% was injected slowly. No evidence of resistance was observed and frequent aspirations were performed to rule out inadvertent intravascular catheter placement.

To realize epidural anesthesia, patient was in a sitting position. Anesthesia was performed on the space between L4 and L5 after anatomical location.

An 18G Tuohy needle with a loss of resistance technique with physiological serum was used. An epidural catheter was placed at 5 cm in the epidural space. Three milliliters of lidocaine with adrenaline 1:200 000 was administrated through the catheter as test dose. Anesthesia was completed with a bolus dose of 10 ml of ropivacaine 0.3% followed by a continuous infusion of ropivacaine 0.3% at 5 mL per hour.

STATISTICAL ANALYSIS

All analyses were conducted with SPSS 20 (SPSS, Chicago, IL, USA).

Intergroup differences were analyzed with an analysis of covariance (ANCOVA) for quantitative variables and chi-square tests for nominal variables. Age and ASA scores were used as covariables. Bonferonni post-hoc tests were used to investigate significant effects.

To investigate potential predictors of different outcomes, linear regressions were applied with age and ASA scores as covariables.

A p-value of .05 was considered significant.

RESULTS

Seventy-two patients were included. Demographics and preoperative characteristics of patients are reported in table 1. The three groups present similar characteristics, except for age (p = .001) and ASA scores (p = .002). Those two variables were therefore added as covariables in further analysis. Preoperative hemoglobin and hematocrit did not differ between groups.

ANCOVA of perioperative variables showed a significant group effect on intraoperative blood loss amount (p = .007) (Fig. 1), intraoperative blood transfusion amount (p = .004) (Fig. 2), consumption of piritramide (p = .01) (Fig. 3) or morphine (p = .002) at day 1 as reported in table 2. Bonferroni post-hocs tests revealed that the lumbar plexus block group significantly differed from the general anesthesia alone group in terms of intraoperative blood loss (p = .007), blood transfusion (p = .004), morphine consumption (p = .003) or piritramide consumption (p = .013). Epidural blockade group showed no differences with general anesthesia alone nor the lumbar plexus block groups. Length of anesthesia or surgery were similar between groups.

For postoperative complications (table 3), lumbar plexus block group had significantly less pulmonary infections (p=.036) (Fig.4) or hypoventilations (p = .022) (Fig. 5) than general
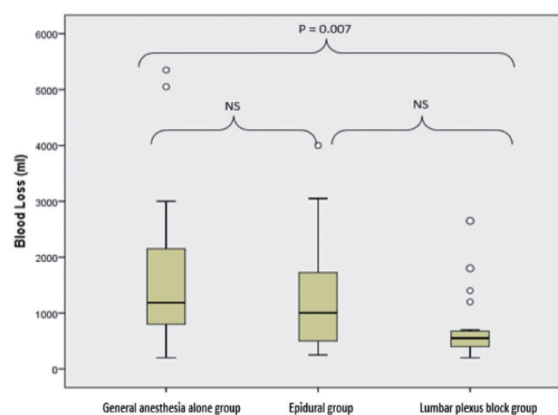

Fig. 1. — Lumbar plexus bloc reduce significantly intraoperative blood loss.
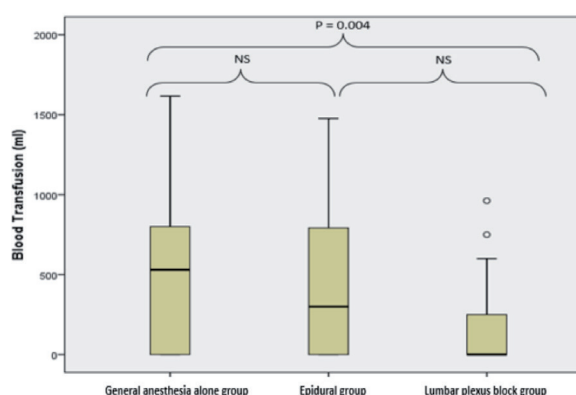

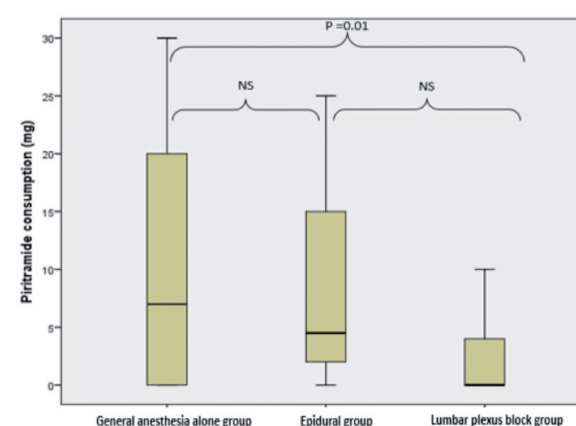Fig. 2. — Lumbar plexus bloc reduce intraoperative blood transfusion.

Fig. 3. — Piritramid consumption was reduced when lumbar plexus bloc was used.

anesthesia alone group. Lumbar plexus block group had more patients without postoperative complication (p = .004) (Fig. 6) than epidural group.

Regressions analysis showed that the type of anesthesia is a predictive factor of intra-

Table 1
Preoperative patients characteristics

	GA n = 26	EPI n = 21	LPB n = 25	P value
Age (years), mean (SD)	59.3 (18.4)	41.0 (14.5)	54.4 (16.8)	0.001
Gender Male/Female	10/16	11/11	10/15	0.587
BMI (kg/m2), mean (SD)	25.1 (5.8)	24.5 (5.3)	23.7 (4.3)	0.636
ASA score : II III IV	9 17 0	19 2 0	14 10 1	0.002
Diabetes mellitus	3	1	1	0.512
Preoperative NSAIDs	1	3	5	0.209
Preoperative Anticoagulants	12	4	11	0.115
Alcohol consumption	9	4	9	0.394
Smoking	5	5	7	0.762
Type of tumors				
Angiosarcoma	0	0	1	0.214
Chondroblastoma	1	0	0	
Aneurismal bone cyst	0	1	0	
Metastasis of cervix cancer	1	1	1	
Metastasis of melanoma	0	2	0	
Metastasis of ovary cancer	0	0	1	
Metastasis of lung cancer	7	4	4	
Metastasis of prostate cancer	0	0	2	
Metastasis of kidney cancer	1	0	2	
Metastasis of breast cancer	8	2	8	
Metastasis of bladder cancer	1	0	0	
Multiple myeloma	1	0	0	
Osteoneobecrosis	0	1	0	
Sarcoma	6	10	6	
Preoperative hemoglobin (g/dl), mean (SD)	11.5 (18)	12.5 (1.8)	11.8 (1.8)	0.145
Preoperative hematocrit (%), mean (SD)	34.5 (5.6)	37.2 (4.8)	36.0 (5.4)	0.216

operative blood loss (p = .002), postoperative respiratory complications (p =.002), respiratory hypoventilations (p = .014), respiratory infections (p =.011) and absence of postoperative complication (p = .002).

DISCUSSION

The progress of oncological medical treatment allows the improvement of the prognosis for primary and metastatic lesions in the proximal femur. This improvement encouraged surgeons to consider limb salvage surgery in most centers as mainstay of treatment for tumors in the lower extremity. Overall patient survival and risk for local tumor recurrence after limb salvage surgery are similar to amputation (2, 22, 23).

Mega prosthetic reconstruction, as limb-salvage surgery, is a widely accepted treatment option after tumor resection and pathological
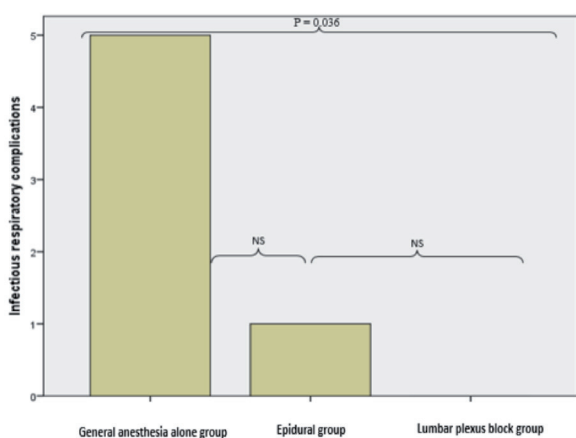
Fig. 4. — Less pulmonary infections were observed when regional anesthesia was used.
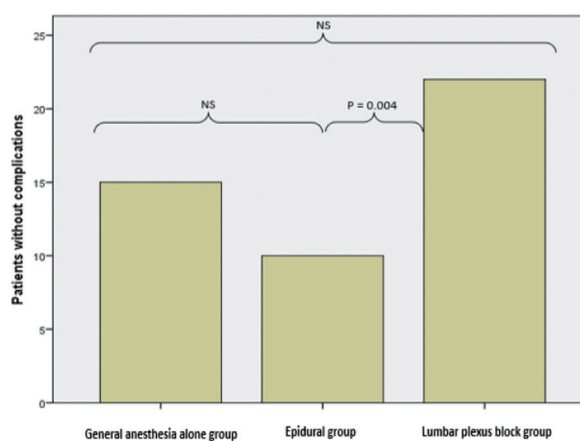

Fig. 6. — Patients without complications were more observed when lumbar plexus bloc was used.
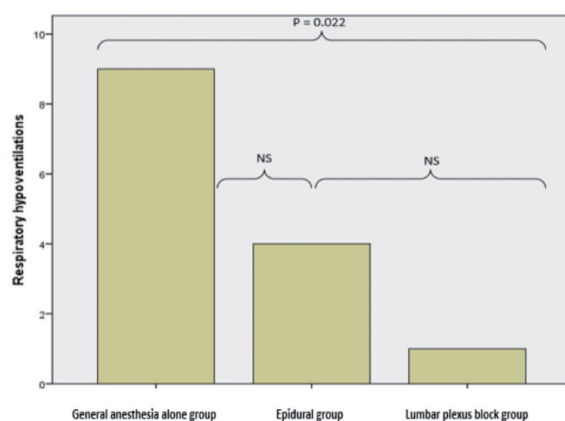

Fig. 5. — Hypoventilations were more observed when general anesthesia was used alone.

Table 2
Intraoperative data

	GA n = 26	EPI n = 21	LPB n = 25	P value
Length of surgery (min) , mean (SD)	201(74)	238 (95)	185 (60)	0.266
length of anesthesia (min), mean (SD)	292 (84)	337 (95)	277 (64)	0.194
Hemoglobin at day 1 in ICU (g/dl) mean (SD)	9.7 (1.1)	9.2 (1.6)	9.8 (1.9)	0.686
Hematocrit at day 1 in ICU (%), mean (SD)	29.4 (3.9)	26.9 (4.9)	29.4 (5.8)	0.358
Intraoperative blood loss (ml), mean (SD)	1651 (1332)	128 (1033)	700 (568)	0.007
Intraoperative blood transfusion (ml), mean (SD)	561 (59)	405 (426)	151 (279)	0.004
Intraoperative Diuresis (ml), mean (SD)	708 (470)	891 (462)	785 (539)	0.346
Crystalloids infusion (ml), mean (SD)	3238(1657)	3714.29 (1270.545)	2937.40 (1114.885)	0.414
Colloids infusion (ml) , mean (SD)	1012(629)	1395 (966)	824 (723)	0.074
Piritramide consumption at day 1 (mg), mean (SD)	10.3(11.2)	7.5 (8.4)	2.1 (3)	0.010
Morphine consumption at day 1 (mg), mean (SD)	9.2 (14.4)	0 (0)	0 (0)	0.002

Table 3
Postoperative outcomes.

	GA	EPI	LPB	P value
Length of hospital stay (day), mean (SD)	35 (32)	27 (21)	27 (21)	0.574
Pulmonary infection	5/26	1/21	0/25	0.036
Hypoventilation	9/26	4/21	1/25	0.022
Pleural effusion	3/26	1/21	3/25	0.659
Postoperative blood loss at day (ml) mean (SD)	311 (216)	672 (516)	287 (236)	0.062
Nausea	4/15	2/10	1/21	0.175
Luxation	1/15	0/10	1/22	0.718
Cardiac complication	1/26	0/21	0/25	0.408
No complication	8/15	5/10	21/22	0.004

* N = 14, ² N = 9, ³ N = 21

fractures of the proximal femur. This technique allows intraoperative modularity with off-the-shelf availability (24, 25, 26), immediate stability and function. Mega prosthetic reconstruction differs from standard allograft reconstructions of malignant lesions of the proximal femur with a reduced bed rest and a faster rehabilitation (27).

Nevertheless, the complications rate of mega prosthetic surgery is approximately 10-fold higher than routine prosthetic reconstructions (28, 29). The complex construction of the implants, the major surgical procedures, and the concomitant morbidities associated with chemotherapy and radiation are factors that predispose patients to an increased complications rate. Indeed, resection of proximal femoral tumors results in major bone and soft tissue loss, blood loss and prolonged LOS (30).

Our study shows that loco regional anesthesia, especially lumbar plexus block, associated to general anesthesia successfully decreased the amount of blood loss and transfusion after modular mega prosthesis for malignant lesions of the proximal femur compared to general anesthesia alone. Our group who received epidural anesthesia associated to general anesthesia did not show a significant reduction of blood loss nor blood transfusion compared to general anesthesia alone. However, the epidural group did not show any significant difference with the lumbar plexus block group. Epidural group appears to be on a continuum between the general anesthesia alone group (highest blood loss and transfusion) and the lumbar plexus block group (lowest blood loss and transfusion), although this is not not significant.

The decreased intraoperative blood loss observed in our study confirms the findings of Twyman et al. (31). Reduced hemorrhage has been documented with various regional anesthetic techniques, including spinal and epidural anesthesia, and is thought to result from attenuated sympathetic tone in medium and small vessels, with concomitantly reduced arterial and venous pressure (32). Two distinct mechanisms may influence blood loss in patients undergoing peripheral or central nerve block: a direct effect on vasoconstrictive sympathetic fibers contained in peripheral nerves and an indirect effect mediated by antinociception and reduced systemic blood pressure.

In a previous study, Stevens et al. , comparing general anesthesia with or without lumbar plexus block, demonstrated lower intraoperative mean arterial pressure in their lumbar plexus block group (equivalent baseline pressure measurements), a similar prevalence of treated arterial hypertension in the two groups, and a lesser administration of isoflurane and fentanyl in the plexus group. The authors concluded that lower mean intraoperative arterial pressure could be attributable to attenuated nociception and autonomic arousal in the block-treated patients (17).

In a recent systematic review for total hip replacement, the authors concluded that blood loss might be decreased in patients receiving regional anesthesia compared to general anesthesia (15).

Therefore, our results confirm the decreased blood loss associated with loco regional anesthesia for lower limb surgery (15, 16, 17, 33, 34). However, we were not able to confirm the usefulness of

Predictive factors for intraoperative blood loss, postoperative respiratory complications and length
of hospital stay

Predictive factors for intraoperative blood loss	F-value	P value
NSIADs consumption	0.719	0.400
Histopathological lesion	0.028	0.868
Anesthesia	10.068	0.002
Anesthesia (AG alone vs AG + regional anesthesia)	6.438	0.014
Anticoagulation	1.404	0.240
Predictive factors for length of hospital stay		
Age	3.238	0.076
ASA score	6.562	0.013
Anesthesia	1.157	0.286
Anesthesia (AG alone vs AG + regional anesthesia)	1.474	0.229
Blood Loss	0.001	0.977
Predictive factors for postoperative respiratory complications		
Tobacco consumption	6.179	0.015
BMI	1.789	0.185
Regional anesthesia	9.934	0.002
Predictive factors for postoperative respiratory hypoventilation		
Anesthesia	8.296	0.005
Anesthesia (AG alone vs AG + regional anesthesia)	6.340	0.014
Predictive factors for postoperative respiratory infections		
Anesthesia	6.604	0.012
Anesthesia (AG alone vs AG + regional anesthesia)	6.743	0.011
Predictive factors for postoperative blood loss		
Anesthesia	0.226	0.637
Anesthesia (AG alone vs AG + regional anesthesia)	0.707	0.405
Predictive factors for absence of complications		
Anesthesia	10.300	0.002
Anesthesia (AG alone vs AG + regional anesthesia)	4.161	0.047

epidural anesthesia associated to general anesthesia in the case of modular mega prosthesis. To our knowledge, this dissociation has not been reported in the literature and comparisons of the two techniques are barely discussed (21). However, a loco regional blockade is more controlled than an epidural, due to neuro stimulation. Indeed, the site of the injection is located by neuro stimulation and the efficiency of the blockade is immediately seen by the loss of contraction of the muscle controlled by the targeted nerve (35). On the other hand, epidural is not so controlled because the epidural infusion starts after the general anesthesia induction. Our results might therefore be explained by a global depreciation of the quality of the epidural compared to the lumbar plexus blockade, due to a lack of controlled efficiency of the epidural.

In addition, loco regional anesthesia was effective for intraoperative pain control. As noted in our results, postoperative morphine and piritramide consumptions were considerably reduced when loco regional anesthesia was used. A statistically significant decrease in overall opioid requirements was noted with the use of lumbar plexus block.

Most randomized clinical trials conclude that the addition of continuous peripheral nerve blockade decreases postoperative pain and opioid related side effects when compared with opioids alone (36, 37). There are several reasons that perineural catheters may provide better postoperative analgesia compared with parenteral opioids, including the fact that local anesthetics may attenuate or block painful input into the central nervous system.

Opioids may also have a role in our observed effects on respiratory complications, since they decrease respiratory rate and promote irregular breathing leading to hypercarbia and hypoxia,

Higher opioids doses in elderly patients change the tidal volume causing hypoventilation and potentially leading to pulmonary infection. Pneumonia is possibly the most important pulmonary outcome in this context since it may increase duration of hospitalization and may lead to death (38).

On the other hand, post-operative pain may be responsible for a short breath with decreased functional residual capacity, and a trend to hypoventilations.

In general, regional anesthesia is appreciated for the superior and long-lasting analgesia they provide (39). Moreover, compared to other types of anesthesia, nerve blocks may decrease risk of urinary retention, a variable not assessed by our study (40). In addition, in the literature, the pelvic location of the primary tumor, the tumor volume and the operative time were found to be independent predictive factor for blood loss (41). The small sample size of our series did not allow to study these factors independently.

LIMITATIONS

As mentioned, a major limitation of our study relies on the quite small sample size of our three groups. Moreover, we observed statistically significant differences between our samples about ASA scores and age, two variables influencing outcomes (42). Specifically, we observed those differences between epidural group and the lumbar plexus block or general anesthesia alone groups. If this discrepancy is probably not responsible for the differences in outcomes observed between

the lumbar plexus block group and the general anesthesia alone group, it may play a role in the evaluated outcomes of the epidural group, as this group is statistically older and presents an worst general physical condition measured by a higher ASA score.

Other limitation is mainly linked to the fact that our study is retrospective. Therefore, some information were missing in the consulted files, limiting the available variables.

Our results need to be reproduced by prospective randomized trials in order to confirm the trends observed in our population.

CONCLUSION

Loco regional anesthesia, especially lumbar plexus block, is an effective complement to general anesthesia and to intraoperative analgesic management of modular mega prosthesis for proximal femoral malignant lesions. This technique reduces blood loss and transfusion during the surgical procedure, opioids consumption and postoperative complications. These findings should be confirmed in large prospective randomized trials. The relatively low number of serious complications demonstrates an adequate preoperative screening and emphasize the importance of adequate maintenance of parameters throughout the perioperative process.

Aknowledgement

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