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Analgesia For Knee Ligamentoplasty Comparisons of Three Techniques Using the Silverman Integrating Approach (SIA SCORE)

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Abstract:

Introduction The aim of this prospective study was to compare the analgesic efficacy of three techniques for knee ligamentoplasty using an integration score, the SIA score.

Hypothesis. The use of a statistical approach to integrate data from pain scores and morphine consumption will identify four patient subgroups that may hamper the accuracy of the comparative study

Material. - We included 165 patients undergoing primary reconstruction of the anterior cruciate ligament of the knee. All patients underwent spinal anaesthesia. The first group, systemic analgesia (SA), received balanced systemic analgesia postoperatively for a minimum of five days, based on Paracetamol, Diclofenac and a morphine PCA. In addition to the systemic analgesia already described, the second group, femoral analgesia (FA), will benefit from a femoral peri-nervous catheter in the crural position. 20 ml of bupivacaine at 0.125% concentration is injected; maintenance is set up immediately with a continuous flow of 8 ml/h for 36 h. The third intra-articular analgesia (IAA) group received, in addition to the same systemic analgesia, an infusion through an epidural catheter of 20 ml of 0.125% bupivacaine, followed by maintenance with 8 ml/h of the same local anesthetic via an electric syringe pump for 36 h. We evaluated cumulative morphine consumption, pain estimation at rest using a numerical scale (EN) from 1 to 10, and an integration of these two parameters.

Results. - The mean age was identical for all three groups, at around 30 years. Analgesia in the femoral peri-nerve group was more effective, with a reduction in mean EN compared with the other two groups. Morphine consumption was lower in the AF group. The lowest mean rank was in the AF group, followed by the AIA group, and the difference was statistically significant with an H = 6.89 and a p= 0.032. The difference was significant between the AS group and the AF group (p = 0.09); the other inter-group differences were not significant. 23.2% of patients had an AIS score between [-100, -200], and were in little pain and consumed little morphine (effective treatment); 14.2% of patients had an AIS score between [100, 200] and were in great pain and consumed a lot of morphine (morphine-resistant or very sensitive to pain). For the difference (ranked pain score - ranked morphine), 4.5% of cases had values between [- 100, - 200] and were therefore not very painful but consumed a lot of morphine (propensity), while 3.9% had values between [100, 200] and were therefore very painful but consumed little morphine (intolerant).

Discussion. - This study suggests that the use of a statistical approach to integrating data from pain scores and morphine consumption, such as the **Silverman Integrating Approach** (SIA), will yield four patient subgroups that may hamper the accuracy of the comparative study, including the morphine-resistant subgroup and the propensity subgroup. Comparison of the means of the therapeutic efficacy group will eventually be more precise. Continuous femoral block really does provide added analgesia and morphine sparing, and should therefore be preferred wherever possible to intra-articular or systemic therapy.

Keywords: SIA score, knee ligamentoplasty, PCA morphine

Introduction:

Reconstructive surgery on the anterior knee ligament is considered one of the most painful procedures, requiring an effective, optimal and well thought-out postoperative analgesic strategy based on available resources.

For our purposes, the most commonly used open technique is the Kenneth Jones (K J), which consists of a free bone-tendon-bone transplant using the middle third of the patellar tendon. (1).

Pain management in the immediate post-operative period and during rehabilitation sessions is therefore a key to success, not forgetting patient comfort and satisfaction, which are increasingly important.

Several classic and conventional analgesic techniques were discussed and compared, taking into account the evolution of technical and pharmacological means in anaesthesia and analgesia whose objective is, on the one hand, to improve patient comfort and, on the other hand, to accelerate postoperative functional recovery. (2)

Peripheral regional anesthesia and analgesia of the lower limb is currently the gold standard in knee surgery (3). Several analgesic techniques and procedures are compared, including femoral nerve block and intra-articular analgesia.

Femoral nerve block, as an analgesia technique, has proven its effectiveness in knee surgery in general, and has become the gold standard (3, 4) .

Continuous administration via catheter in major knee surgery is justified on two grounds: the deep branches (nerves of the quadriceps femoris and saphenous vein) are involved in the innervation of the knee joints (5) and the reflex contracture of the quadriceps muscle, which is extremely painful and limits post-operative rehabilitation. This explains the interest of the femoral catheter for analgesia and rehabilitation in this context (6). The usual basic flow rate is 0.1 ml/kg/h. It can be modulated secondarily according to the quality of analgesia obtained (3).

Intra-articular analgesia is an analgesia technique mainly developed for endoscopic knee surgery, but with indications for all joints (2, 3). It represents an alternative to femoral peri-nervous block for analgesia during knee surgery. Defined as the injection of analgesic molecules into the joint capsule to treat acute pain, and conceptually based on the presence of receptors or axonal endings of nociceptive neurons (2) sensitive to various stimuli, tension, traction, and particularly to inflammatory mediators.

Intra-articular injection of bupivacaine at the end of the procedure has been shown to be beneficial, both in terms of pain reduction in the first 6 hours, and in terms of sparing associated analgesics (7-9).

Prolonging intra-articular analgesia with a catheter, positioned by the surgeon at the end of the procedure, is a simple technique that has proved effective (10).

In clinical pain trials, the use of PCA morphine can lead to false-positive results when comparing different techniques. It is not ethical to deprive patients of this tool in order to compare different techniques.

The use of morphine in self-monitoring may give rise to subgroups of patients who may hamper the accuracy of the comparative study, including a subgroup of morphine-resistant patients and a subgroup of patients who use morphine for purposes other than pain. The use of a statistical approach to integrating data from pain and morphine consumption scores, such as the "**Silverman Integrating Approach**" (SIA), makes sense.

The aim of our work is to compare these three analgesic techniques using this approach. The objectives of this prospective randomized study are:

- The analgesic efficacy of each technique.
- Study of patient subgroups.

Materials and methods:

This was a prospective, comparative, randomized, single-center study conducted over three years in the orthopedics and traumatology unit of the Sétif hospital.

Population:

A population of adults admitted during the study period for primary reconstruction surgery of the anterior cruciate ligament of the knee.

Inclusion criteria:

- Consenting patients.
- Admitted for rupture of the anterior cruciate ligament of the knee.

Exclusion criteria :

- Patient refusal
- Surgical revision
- Alternative indications for ALR
  - Local or systemic infection,
  - Patient on anticoagulants,
  - Allergy to local anaesthetics...
- Contraindications to non-steroidal anti-inflammatory drugs

Population size :

During the study period, 173 patients were admitted for knee ligamentoplasty, of whom eight were excluded: five refused spinal anaesthesia, two repeat surgeries and one contraindication to diclofenac.
The minimum sample size required was 33 patients in each group.

Methods :

A total of 165 cases were included, divided into three study groups by drawing lots:

- 1st group (AS): patients receiving systemically balanced analgesia (paracetamol + diclofenac + PCA morphine)

- The 2nd group (AF): patients receiving, in addition to "paracetamol, Diclofenac and PCA morphine", continuous femoral peri-nervous analgesia.
- The 3rd group (AIA): patients receiving, in addition to "paracetamol, diclofenac and morphine PCA", continuous intra-articular analgesia.

Study protocols:

Intra-anaesthetic stage:

After the patient is settled in and standard monitoring is performed, a solid venous line is taken and prefilling is started. Spinal anesthesia is performed with 12.5 mg bupivacaine 0.5% + 25 δ clonidine. Antibiotic prophylaxis with 2g cefacidal is administered.

Procedures:

After surgery, patients were clearly informed of the three analgesic procedures, and informed consent was obtained:

- The first group (AS) will receive systemically balanced analgesia postoperatively for a minimum of five days, based on :
- Paracetamol at a dose of 1g every 6h per os.
- Diclofenac 50 mg every 12 hours per os.
- And a morphine PCA with a concentration of 1mg /ml and a refractory period of 7 min.
- In addition to the systemic analgesia already described, the second group (AF) will benefit from a femoral peri-nervous catheter in the crural position for a minimum of five days, with the same dosage:

After locating the femoral nerve by ultrasound, and dilating the space with a few milliliters of saline, a 5-8 cm catheter is inserted.

20 ml of bupivacaine at a concentration of 0.125% is injected fractionally through the anti-bacterial filter;

Maintenance is started immediately with a continuous flow of 8 ml/h of the same anesthetic via an electric thumb syringe, for 36 h.

- The third group (AIA) will receive, again in addition to the same systemic analgesia already described, through an epidural-type catheter placed intra-articularly by the surgeon at the end of the procedure after closure of the joint capsule and mounted 5 to 8 cm and securely fastened.

20 ml bupivacaine 0.125% is injected through the antibacterial filter 10 to 15 min before deflating the pneumatic tourniquet, with the Redon drain still clamped. Maintenance is also started immediately with 8 ml/h of the same local anesthetic via an electric syringe pump for 36 hours.

Intra-articular catheters are practically removed at the same time as the Redon drain at D2 post-op, as are peri-nerve catheters.

Intravenous analgesia (paracetamol + diclofenac) is continued for a minimum of five days, beyond which the continuation of analgesic treatment is self-controlled.

Data from :

- In the immediate postoperative period and until catheter removal, by the following judgment criteria:

- Quantitative: cumulative morphine consumption
- Qualitative: estimation of pain at rest and on mobilization using a numerical scale (EN) from 1 to 10.

Data will be collected on a data sheet at h2, h4, h6, h8, h12, h16, h20, h24, h28, h36, h2, h3, h4 and h5. (T0: injection of local anesthetic for both the AF and AIA groups, and the patient's installation at the post-operative level for the AS group).

Statistical analysis :

Results are analyzed using SPSS statistics 26 software. We use both descriptive and analytical statistical techniques.

Descriptive statistics :

- Tabular and graphical presentation.
- Reduction parameters (mean and standard deviation).
- Frequency and percentage for qualitative variables

Analytical techniques :

Statistical significance tests for the comparative study :

- Reduced deviation test for comparing proportions and means.
- ANOVA variance test for comparison of more than two groups, completed by post-hoc tests.
- Chi-square test for repeat comparison.
- Non-parametric test for K independent samples (Kruskall-Wallis and Mann-Whitney) for the integration score of pain and morphine consumption scores (SIA score).

Results will be considered significant for a $p \leq 0.05$.

Statistical approach to integrating pain score and morphine consumption data: Silverman Integrating Approach (SIA)

This approach involves ranking the pain and morphine consumption scores, then calculating the sum and difference of the percentage ranks of each parameter so that they can be statistically interpreted. (11).
Results:

Population :

The average age was identical for all three groups, at around 30 years (ANOVA: $F = 0.335$, $p = 0.716$) (Table 1).
We note that the difference was not significant between the two genders in the three groups (Chi2 = 0.512, $p = 0.774$).
The AF and AIA groups each had 03 cases of ASA 2, compared with only 01 in the AS group, but the difference was not statistically significant, with a Chi-square = 1.193, $p = 0.551$.

Table 1Demographic data by study group.

Groups	Total (N = 165)	Systemic balanced analgesia(n =55)	Femoral peri-nerve (n=55)	Continuous intra-articular (n=55)	P
Age	30,00 ± 7,30	29.36 ± 6.745	30.16 ± 7.932	30.47 ± 7.280	0.716
Gender : Male : Female :	 (161) 97,6% (04) 2,4%	 33,5% (54) 25% (01)	 32,9% (53) 50% (02)	 33,5% (54) 25% (01)	0,774
ASA : ASA 1 : ASA 2 :	 (158) 95,8% (07) 4,2%	 (54) (01)	 (52) (03)	 (52) (03)	0,551

Pain assessment :

Postoperative pain assessment, at rest using a numerical scale from 0 to 10, was collected repeatedly from the second hour to the fifth day .

From H2 to D5 post-operatively, the means with standard deviations for EN are summarized in Table 2

Table 2 Means with standard deviations of EN at rest by group

	Total	AS Group	AF Group	AIA Group	p
H2	0,72(1,66)	0,67(1,41)	1,08(2,31)	0,44(0,99)	NS
H4	2,19(2,10)	2,45(2,21)	1,65(1,89)	2,42(2,12)	**NS 0.084**
H6	3,52(2,32)	3,50(2,39)	3,12(2,38)	3,91(2,16)	NS
H8	3,54(2,49)	3,52(2,47)	3,16(2,39)	3,91(2,59)	NS
H12	2,29(2,26)	2,58(2,36)	2,27(2,35)	2,04(2,26)	NS
H16	1,63(1,92)	1,98(2,11)	1,49(1,95)	1,42(1,68)	NS
H20	1,38(1,79)	1,60(1,79)	1,18(1,64)	1,35(1,93)	NS
H24	1,11(1,55)	1,49(1,64)	0,69(1,30)	1,11(1,59)	**0,034**
H28	0,90(1,36)	1,24(1,52)	0,59(1,08)	0,85(1,36)	**NS 0.063**
H36	0,80(1,56)	1,26(2,04)	0,46(1,22)	0,61(1,13)	**0,03**
J2	0,87(1,43)	1,06(1,53)	0,75(1,41)	0,78(1,36)	NS
J3	0,61(1,29)	0,62(0,86)	0,45(1,13)	0,72(1,72)	NS
J4	0,57(1,38)	0,60(1,25)	0,20(0,56)	0,84(1,85)	NS
J5	0,57(1,48)	0,69(1,36)	0,41(1,33)	0,58(1,72)	NS

Morphine consumption:

Morphine consumption according to the three study groups is shown in Table 3;

Consumption was lower in the AF (femoral peri-nerve) group and the difference was statistically significant with an $F = 3.539(2)$ and a $p = 0.031$.

The post-hoc test shows a difference in mean of 6.12 ± 2.41 between the AS and AF groups with a significant $p = 0.012$, a difference in mean of 1.67 ± 2.41 with a non-significant $p = 0.49$ between the AF and AIA groups and a difference in mean of 4.45 ± 2.31 with a p = 0.056 at the limit of significance between the AS and AIA groups.

Table 3 Comparative averages of morphine consumption as a function of time.

	AS Group		AF Group		AIA Group		P
	Average	Standard deviation	Average	Standard deviation	Average	Standard deviation	
H2	0,57	1,52	0,61	1,18	0,2	0,55	0,134
H4	2,12	2,78	1,5	2,49	1,4	1,91	0,243
H6	2,74	2,51	2,37	2,82	2,30	2,87	0,681
H8	2,86	2,84	1,60	2,04	2,66	2,59	0,041
H12	3,77	5,12	2,20	2,88	2,84	3,60	0,165
H16	2,41	3,10	1,45	1,83	1,32	1,62	0,037
H20	1,60	2,69	1,63	3,53	0,96	1,83	0,372
H24	1,02	1,60	0,72	1,51	0,84	2,13	0,735
H28	0,69	1,19	0,74	1,42	1,22	3,08	0,409
H36	1,57	3,71	0,48	0,88	0,73	1,11	0,088

Integrated assessment of pain scores and morphine consumption :

For the SIA score (sum), patients in the range [100, 200] have more pain despite the use of more morphine; this is morphine resistance or very high pain sensitivity.

Patients in the [-200, -100] range have less pain for less morphine consumption;

As for the difference, patients in the [-200, -100] range have little pain and consume a lot of morphine; this is known as drug propensity.

Patients in the [100, 200] range are very painful, consume little morphine and are morphine-intolerant ;(Figure 3)

Figure 3 SIA score interpretation diagram.

Overall SIA at rest :

23.2% of patients had an AIS score between [-100, -200], and were in little pain and consumed little morphine (effective treatment), including 38.9% in the AIA group but without statistical significance;

14.2% of patients had an AIS between [100, 200] and were very painful and consumed a lot of morphine (morphine-resistant or very sensitive to pain), including 50% in the AS group. But the difference was not significant with a Chi-2 = 5.63 and a p = 0.228 (Figure 4 and Table 4).

For the difference (ranked pain score - ranked morphine), 4.5% of cases had values between [-100, -200] and were therefore not very painful but consumed a lot of morphine (propensity), 42.9% (03 cases/07) of which were in the AF group, but the difference was not significant;

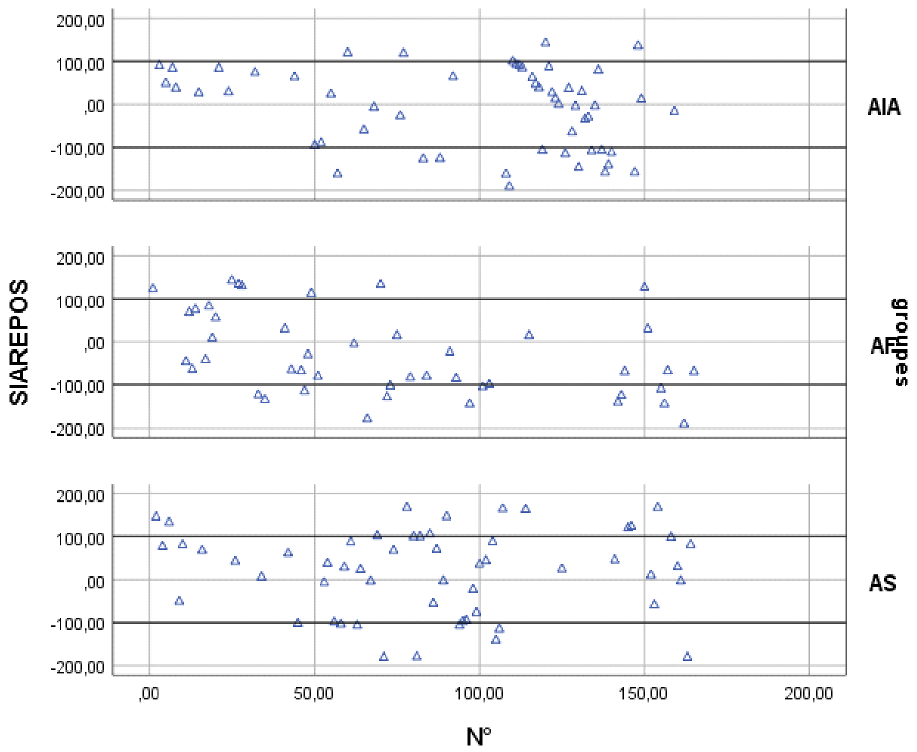

Figure 4 AIS score at rest

While 3.9% had values between [100, 200] and were therefore very painful but consumed little morphine (intolerant), 66.7% (4 cases/6) were in the AIA group and the difference was not significant with a chi-square = 4.67, p = 0.323 (Figure 5 and Table 5).

Table 4 Percentage of SIA score extremes and difference

		[-200 ; -100]	[100 ;200]
SIA score	Comments	Therapeutic efficacy	Morphine resistance or exaggerated pain sensitivity
Difference	Comments	Propensity for drugs	Intolerance
H6	SIA score	19%	13,10%
	Difference	3,90%	6,50%
H12	SIA score	17,80%	12,50%
	Difference	4,60%	5,30%
H24	SIA score	21,90%	15,90%
	Difference	3,30%	5,30%
H36	SIA score	38,20%	9,60%
	Difference	2,90%	0,70%
Global	SIA score	23,20%	14,20%

	Difference	4,50%	3,90%

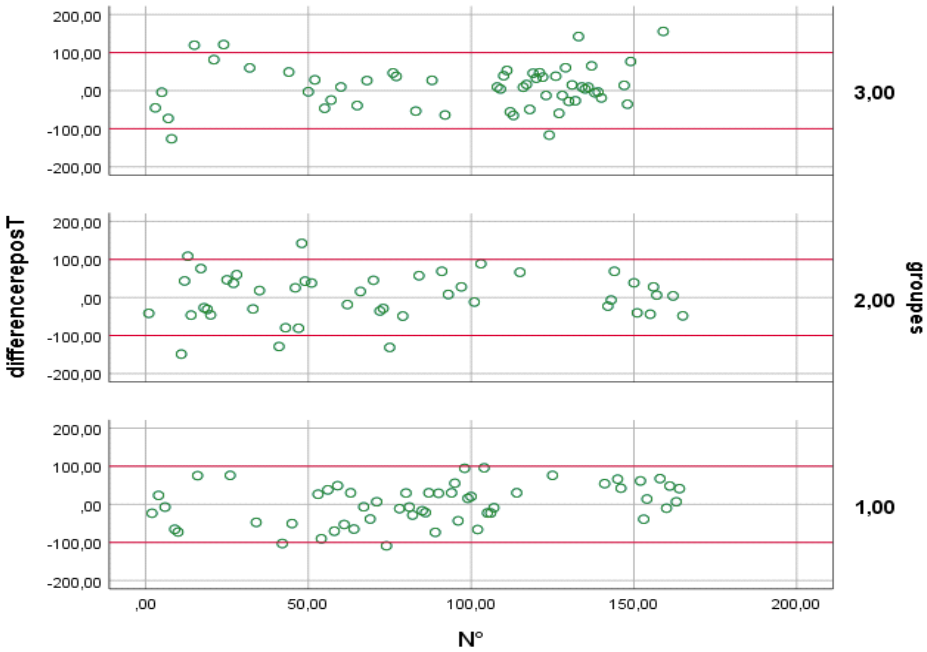

Figure 5 Differences in pain scores and morphine consumption

Table 5 SIA and percentage differences by group

		AS Group		AF Group		Group AIA		P
		[-200 ; -100]	**[100 ;200]**	**[-200 ; -100]**	**[100 ;200]**	**[-200 ; -100]**	**[100 ;200]**	
H6	**SIA score**	**31%**	**45%**	**34,50%**	**30%**	**34,50%**	**25%**	**NS**
	Difference	**50%**	**40%**	**33,30%**	**10%**	**16,70%**	**50%**	**NS**
H12	**SIA score**	**29,60%**	**52,60%**	**37%**	**15,80%**	**33,30%**	**31,60%**	**NS**
	Difference	**71,40%**	**12,50%**	**0%**	**25%**	**28,60%**	**62,50%**	**NS**
H24	**SIA score**	**27,30%**	**45,80%**	**30,30%**	**25%**	**42,40%**	**29,20%**	**NS**
	Difference	**20%**	**25%**	**60%**	**37,50%**	**20%**	**37,50%**	**NS**
H36	**SIA score**	**32,70%**	**69,20%**	**30,80%**	**0%**	**36,50%**	**30,80%**	**5,20 %**
	Difference	**0%**	**0%**	**50%**	**100%**	**50%**	**0%**	**NS**
Globa	**SIA**	**25%**	**50%**	**36,10%**	**31,80%**	**38,90%**	**18,20%**	**NS**

l	**score**							
	Difference	**28,60%**	**0%**	**42,90%**	**33,30%**	**28,60%**	**66,70%**	**NS**

SIA and gender :

Comparison of the global SIA score at rest on a Mann-Whitney test had found a mean rank of 77.32 in males and 112.67 in females, but the difference was not significant with a U = 124.00 and a P = 0.177 ;

SIA and age:

The under-30s had a mean rank of 88.09 vs 62.03 for the over-30s at rest, and 88.54 vs 60.21 at movement and the difference was statistically significant, with a $p < 0.0001$. The WMWodds = 0.32 ± 1.10.

SIA and study groups :

Table 6 Characteristics of the global AIS score at rest

N	Average	Standard deviation	Min	Max	Percentiles		
					25e	50th (median)	75e
155	-5,35	96,86	-190,96	166,86	-97,58	8,43	78,90

The median global AIS score at rest was 8.43 ;(Table 6)

On a Kruskal-Wallis test, the lowest mean rank was in the AF group, followed by the AIA group, and the difference was statistically significant with an H = 6.89 and a p= 0.032.

The median test found a Chi-2 = 7.35 and a p = 0.025.

On a post-hoc test, the difference was significant between the AS group and the AF group (p = 0.09).

Other inter-group differences were not significant (Figure 6).

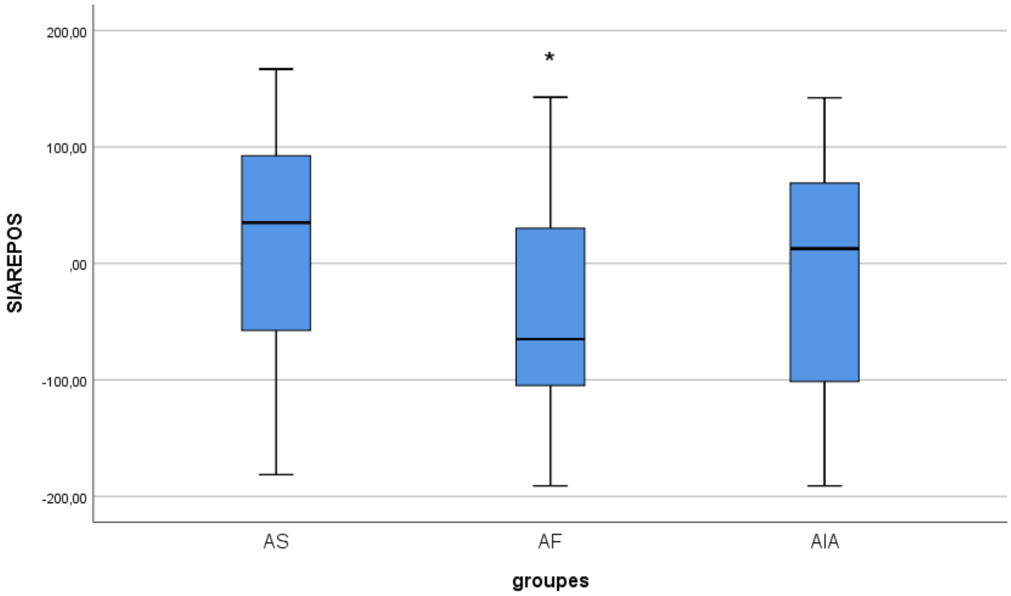

Figure 6 Difference in overall resting averages for rows by group

(*) : $p < 0.05$ between AS and AF groups.
The difference was not significant between the AS and AIA groups, $p = 0.192$.
And the difference was not significant between the AF group and the AIA group $p = 0.195$.

Discussion:

Digital scale and ALR procedures :

Analgesia in the femoral peri-nerve group was more effective, with a reduction in mean EN compared with the other two groups.
Efficacy was statistically significant at H4, then from H24 to H36 compared with systemic analgesia, but not significant compared with intra-articular analgesia.
Intra-articular analgesia was only significantly more effective than systemic analgesia at H36; this may be due either to the low concentration of LA (0.125), or to the absence of morphine-type adjuvants that could potentiate analgesia, or to the absence of associated infiltration of the surgical site.

The efficacy of femoral block in knee surgery is indisputable in the literature, which still considers it the gold standard; this is the case of the Williams studies(12) and Frost(13) and many other studies (14-18).
Continuous block is more efficient than single or sequential injection(19, 20) .
In the Harris study, comparing a femoral nerve block group with a control group, pain scores were significantly reduced only at H24 post-operatively(14) ;
In Ren's 2015 study(21)comparing 280 patients in two study groups: continuous femoral block and morphine PCA, for knee arthroplasty, the effectiveness of continuous femoral block during the procedure was significantly superior in terms of pain score and morphine consumption.
But other studies also found no significant reduction in pain scores compared with control groups; such as the Matava study (22)and O'Leary(23).

In the literature, the efficacy of intra-articular knee analgesia also varies from one study to another.
In fact, several methods of administering LAs and adjuvants have been evaluated;
Infusion of AL solution alone into the joint cavity for analgesia is a rare procedure.
Infiltration of the surgical site and the addition of morphine or other substances to AL was the most debated technique.
In a study comparing the quality of analgesia from an intra-articular injection of 0.5% bupivacaine alone and pethidine alone and their combination, the EVS in the bupivacaine alone group was 20±8 mm at H6 and H12, and the quality and time of analgesia were better in the bupivacaine + pethidine group (24).
In Alford's study comparing a 0.025% bupivacaine infusion to placebo for ACL treatment (25) the median NE (at 2.5) was significantly reduced in both groups compared with a control group (at 4), and was comparable between the two groups, while the maximum NE (4.5 vs. 6) was reduced in the bupivacaine group.
In Parker's study (26)no significant difference in pain scores was found between the bupivacaine, placebo and control groups (3.33±1.96 vs. 2.93±1.93 vs. 3.93±2.04); apart from greater morphine consumption in the control group.

On the other hand, infiltration of the surgical site and the addition of morphinics to the LA solution gave better analgesia; this was the case in the studies by Imani (24)and HÖher(27)Hoenecke (28)by Karlsson(29)and Koh(30).

Morphine consumption and ALR procedures:

Femoral perianalgesia provided considerable morphine savings compared with systemic analgesia (6.12±2.41; p = 0.012).

An expected result that parallels the reduction in pain scores in this group, already discussed above.

This saving should perhaps have been greater with a higher concentration of bupivacaine, and with a lower fraction of mechanical incidents causing secondary failure.

In fact, all the studies mentioned above point to a reduction in the consumption of morphine and analgesics;

In a recent meta-analysis, comparing the association of femoral block with systemic analgesia to systemic analgesia alone, the authors conclude that femoral block decreases, but slightly, morphine consumption in the first 24 hours (31).

In a Cochrane database, a meta-analysis looked at femoral block in major knee surgery (32) In 12 studies comparing single-injection femoral block with PCA morphine, the reduction in consumption at 24 hours was -12.86 [-18.65, -7.08];

In 08 studies conducted for the comparison of continuous femoral block vs PCA morphine at 24h, morphine consumption was reduced by -16.89 [-24.01, -9.77]

Citing Chan's 2013 study in detail (33)where the average difference in 24h consumption was -29.70 [-38.59, -20.81] and Kadic's 2009 study (34) with a mean difference of -13.00 [-20.16, -5.84] , and that of Baranovic in 2011 (35) with a mean difference of -25.00 [- Intra-articular analgesia resulted in morphine savings of 4.45 ± 2.31 mg with a p = 0.056.

Consumption was lower, especially in the first 06 hours, and from H12 to H24 (especially H16).

Increasing the concentration of LA and/or adding morphine could reinforce this sparing.

Few studies used intra-articular infusion alone as an analgesic technique, In a meta-analysis of intra-articular analgesia in arthroscopic knee surgery including 20 studies (36)12 studies showed pain relief after intra-articular local anesthesia in at least one of the pain parameters considered, while the other eight studies showed no such improvement.

In 09 studies, morphine consumption was significantly reduced by 10-50% within 4 hours.

Morphine reduction in AIA is a reality. But in Parker's study (26)the authors did not find a statistically significant difference in overall morphine consumption between the continuous intra-articular group, the placebo group with saline infusion, and the control group;

A single significant difference in morphine consumption with a p = 0.015 was found between the AIA group and the control group from 48 h to 72 h in the time-dependent analysis.

28.68, -21.32].

In Joshi's study (8) the analgesia provided by the injection of 20 ml of bupivacaine did not exceed 4 h, and gave a reduction in morphine consumption compared with a control group.

In the same study, morphine alone or combined with bupivacaine reduced morphine consumption and pain scores more, and for longer.
In Musil's study (37) on 85 ACLs divided into 05 study groups with and without intra-articular injection of a mixture combining bupivacaine + morphine + adrenaline, the authors reported a 29% reduction in morphine consumption compared with the control group.
In Guler's study (38)the authors used a mixture of bupivacaine and morphine intra-articularly and compared their efficacy as a function of the injection time before or after deflation of the pneumatic tourniquet, concluding that the reduction in pain scores and morphine consumption was more pronounced in the group after deflation of the tourniquet.
Alford's study (25) and Hoenecke's study (28)using continuous infiltration of the surgical site after intra-articular injection of AL, found a reduction in morphine consumption, but not significant in the Alford study, and 37%, $p < 0.05$ in the Hoenecke study.

Integrated assessment of pain scores and morphine consumption: the SIA score :

In clinical trials on pain, the use of PCA morphine can lead to false positive results when comparing several techniques, whereas depriving patients of this tool in the interests of comparing different techniques is unethical. (39).
The use of morphine in self-medication may give rise to four subgroups of patients that may hamper the accuracy of the comparative study, including a subgroup of morphine-resistant patients and a subgroup of patients who use morphine for purposes other than pain.

Effectiveness of analgesic techniques :

Overall, the very good efficacy of the analgesic techniques compared was observed in 23.2% of cases, and was better in the AIA then AF group, but without statistical significance.
Following the kinetics of pain and morphine consumption at peak times (H8 -H12), the efficacy of FA was better.
In this vision, the perfect efficacy of ALR cannot be asserted.
An improvement in practices, with fewer incidents in the AF group, a source of secondary failures, and the addition of infiltration of the surgical site and molecules potentiating the effect of LA in the AIA group, could perhaps give a significant difference in favor of the ALR techniques introduced.

Morphine resistance or exaggerated sensitivity:

14.2% of patients were morphine-resistant or had increased pain sensitivity. This resistance was more marked in the AS group, which had consumed the most morphine overall.
We believe we are dealing with patients with tolerance and secondary hyperalgesia following previous opioid use (codeine-type), or with disafferent pain that is naturally morphine-resistant.
Post-operative acute morphine tolerance has even been described in the literature(40-42) ;
In Chelly's study (43) study, used as an example to detail Silverman's approach to integrating pain and morphine consumption scores (39) the calculated fraction of morphine-resistant patients was 13.46%.

Propensity for drugs:

Overall, the propensity concerned 4.5% of cases; Together with young age, these two parameters may explain the high consumption of morphine in our study among the under-30s.

But despite this propensity rate, age remains a predictive factor for morphine consumption and increased pain, with 32% evidence.
Another factor that may explain the high morphine consumption despite mild pain is the use of PCA for anxiolysis and mood described in the studies by Taenzer (44) and Robert (45) where they found a strong correlation between morphine consumption and the degree of anxiety and mood, compared with a weak correlation between morphine consumption and the degree of pain.
In the Chelly study, the calculated fraction of patients with morphine propensity was 9.61%.

Morphine intolerance:
Intolerance concerned 3.9% of cases, and may be correlated with the side effects of morphine, a source of reluctance to self-inject.
In Chelly's study, the calculated intolerance was 5.76%;
In an international cohort study of the side effects of morphine drugs used to treat acute pain in emergency departments (46)the authors reported a 25% rate of side effects, and 4.7% of the cohort had required suspension of treatment defining intolerance.

Comparison of AIS scores by group:
Overall, femoral peri-nerve was better in terms of analgesia and morphine sparing, followed by intra-articular analgesia;
The difference is significant between AF and AS, but not between the other comparisons.
This difference is significant only at H12, where statistical tests show the superiority of FA over the other two techniques; the difference between AIA and AS is not significant.
These results adhere to those of several studies already debated, and we believe that our AIA, as practiced, is insufficient to cover the pain of ligamentoplasty.

Conclusion:
The use of a statistical approach to integrate data from pain and morphine consumption scores, such as the **Silverman Integrating Approach** (SIA), will identify four patient subgroups that may hamper the accuracy of the comparative study, including the morphine-resistant subgroup and the propensity subgroup. The comparison of means in the therapeutic efficacy group will be more precise and free of false positives.
Continuous femoral block really does offer an added benefit in terms of analgesia and morphine sparing, and should therefore be preferred wherever possible.
It is difficult to choose intra-articular analgesia over systemic analgesia via the general route ; the theoretical risk of infection and chondrotoxicity of the former, and the simplicity of the latter, makes us lean towards systemic analgesia, unless AIA is optimized and supplemented by infiltration of the surgical site.
The choice of one technique or the other depends on material and human resources, and on the risk/simplicity ratio.

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