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The cumulative analgesic consumption score (CACS): evaluation of a new score to describe postsurgical analgesic consumption as a surrogate parameter for postoperative pain and invasiveness of surgical procedures

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ABSTRACT

Objective: To validate and evaluate the applicability of a new score to describe postsurgical analgesic consumption in urological and surgical patients across different categories of pain medications and the invasiveness of medical interventions.
Materials and Methods: The cumulative analgesic consumption score (CACS) was determined for two cohorts of patients split into three groups with surgeries involving clinically distinct levels of invasiveness (n = 2 x 60). Nonparametric statistical analyses were performed to determine differences between the CACS among the different groups and to assess the correlation between CACS and numeric rating scale (NRS) values for pain intensity.
Results: The score was determined for postoperative days 1 and 2 and revealed median scores of 0 (0-11), 3 (0-22) and 10 (6-17) for UA (urological patients from group A), UB (group B) and UC (group C), respectively, and 4 (0-20), 8 (0-38) and 17 (7-68) for SA (surgical patients from group A, SB (group B) and SC (group C), respectively. CACS enabled reliable differentiation between groups involving different levels of invasiveness ($p < 0.001$). CACS and peak NRS values showed variable degrees of correlation, as expressed by levels of significance ranging from $p < 0.001$ to $p = 0.34$ (NS).
Conclusions: The CACS is a valid and easily applicable tool to describe postsurgical analgesic consumption in urological and surgical patients. It can be used as a surrogate parameter to assess postsurgical pain and the invasiveness of surgical procedures. These aspects may be measured to compare surgical procedures, in both clinical trials and clinical practice settings.

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INTRODUCTION

Following the development of minimally invasive surgery, measurements of invasiveness have become an issue of increasing scientific interest, particularly in parallel group trials comparing interventional and surgical treatments, such as laparoscopic and open surgery (1-4). Postoperative pain

correlates with the severity of impairment of bodily integrity, and hence with the invasiveness of surgical interventions. We hypothesize that pain and postoperative analgesic consumption (AC) constitute non-invasive measurement tools for surgical invasiveness when compared with other determinants of invasiveness such as inflammatory and immunologic markers (5).

Evaluation of pain is usually accomplished using numerical methods of pain measurement such as a visual analog scale (VAS) or a numeric rating scale (NRS). These have been widely accepted as patient-reported outcome (PRO) measurement tools and are commonly used in clinical trials and clinical practice settings to assess pain intensity (6-8). However, numerous confounding factors influence sensations of pain, and no agreement has been reached as to which is the gold standard method for assessing pain (9).

AC is a clinically reported outcome (CRO), which can be used as a surrogate parameter for postoperative pain (2) and analgesimetry (10,11). However, data establishing the validity of AC as a CRO in clinical trials on interventional and surgical treatments are scarce, and no generally applicable scheme has been established to evaluate AC (2). Comparisons in postoperative AC are usually conducted by counting doses of a defined drug (12,13), computed morphine equivalents (14) or patient-controlled analgesia (PCA) (15).

The cumulative analgesic consumption score (CACS) was developed in cooperation with the Department of Anesthesiology. It integrates a classification of AC by potency (qualitative) and by dose measurement (quantitative). The qualitative assessment is based on a modified version of the WHO pain relief ladder (WHO I - III) (16,17), which disregards the administration of any adjuvant medications. The quantitative assessment is carried out by summing up single administrations, but not individual doses, of a certain drug. Computed values for each WHO category are counted to obtain the CACS for an individual patient. As a mathematical formula the CACS may be expressed as:

An adequate timeframe must be defined, e.g., postoperative days 1 to 3 after minor surgery or postoperative days 1 to 8 after major surgery. The index is conceived as an open-ended scale that can be used for different timeframes.

MATERIALS AND METHODS

Informed consent requirements for this retrospective study were approved by the local ethics committee and were therefore performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The CACS was determined for two cohorts of urological and surgical patients (n = 2 x 60). Each cohort was split into groups that received surgical treatments of different invasiveness from a clinical standpoint. Urological patients from group A (UA) had received interventions such as the insertion of an ureteral stent or a percutaneous nephrostomy tube; those of group B (UB) had undergone transurethral resection of the bladder or prostate, ureteroscopy or surgery of the external genitalia; and those of group C (UC) (18) had been treated by laparoscopic or open surgery of the kidney, bladder or prostate. Surgical patients from group A (SA) were those that had undergone minor surgery such as appendectomy or hernia repair; those of surgical group B (SB) were patients who had undergone medium scale surgical interventions such as cholecystectomy or thyroidectomy, and those of group C (SC) were patients who had undergone major surgery, e.g., hemihepatectomy or rectal resection. The timeframe for CACS determination was defined as the first two postoperative days, as this was the minimum duration of inpatient stay for all patients. Patients received preemptive/baseline and on-demand analgesic medications, according to standard protocols for medium or major surgery, or on-demand medications for minor interventions. Based on the WHO pain relief ladder (15,16), specified protocols for various surgical procedures included the following drugs: step 1 (non-opioids): acetaminophen, ibuprofen or metamizole; step 2 (opioids for mild to moderate pain): tramadole,

Σ = n x step of WHO pain relief ladder

e.g.: 2 x WHO step III + 3 x WHO step II + 5 x WHO step I = 6+6+5 = CACS 17

tilidine/naloxone; and step 3 (opioids for moderate to severe pain): piritramide, pethidine, oxycodone or morphine. Patients treated with PCA or regional anesthesia and patients on analgesic long-term medication were excluded from the study.

All patients were asked to indicate their subjective sense of pain on an NRS (ranging from 0 = "no pain" to 10 = "worst possible pain"). Pain was assessed three times a day at rest and (if possible) after mobilization for the first two postoperative days, and if the patient expressed extensive pain. NRS and CACS scores were retrospectively determined based on data obtained from the electronic patient records of our department.

The primary objective of the study was to confirm if there were significant differences in CACS values between groups SA, SB and SC and between groups UA, UB, UC (as assessed by the Kruskal-Wallis test and Mann-Whitney test). The secondary objective was to confirm if a high correlation existed between CACS (objective measurement of analgesic consumption) and NRS values (subjective pain sensation) for each group, using Spearman's rank-correlation test.

RESULTS

Review of patients' records enabled retrieval of all necessary values, with no missing data.

CACS values ranged from 0 to 11 (median 0) for group UA, from 0 to 22 (median 3) for group UB, and from 6 to 17 (median 10) for group UC; in the surgical cohort, values ranged from 0 to 20 (median 4) for group SA, from 0 to 38 (median 8) for group SB, and from 7 to 68 (median 17) for group SC. Statistical analysis confirmed the ability of CACS to differentiate reliably between groups involving different levels of invasiveness (p-values < 0.001). In contrast, this was not true in the same way for corresponding mean and peak NRS values for pain sensation (p-values ranging from "non significant" (NS) to < 0.005) (Table-1).

Comparison of CACS and peak NRS values revealed variable correlations, as expressed by levels of significance ranging from p < 0.001 for UA and UB to p = 0.21 (NS) for UC, and from p < 0.001 for groups SA and SB to p = 0.34 (NS) for group SC (Table-2).

DISCUSSION

The presented data demonstrate the clinical applicability of a newly developed score to determine postsurgical analgesic consumption. Given that pain and AC stand in a close correlation to the invasiveness of a specific procedure, our data suggest a stronger correlation between CACS values

Table 1 - CACS values and corresponding NRS values for pain (urological and surgical patients).

Patient group (3 x n = 20)	CACS (median, range)	NRS mean (median, range)	NRS peak (median, range)
UA (minor surgery)	0 (0 – 11)	0 (0 – 2.50)	0 (0 – 7)
UB (medium scale surgery)	3.00 (0 – 19)	1.0 (0 – 3.75)	2.0 (0 – 8)
UC (major surgery)	10.0 (6 – 17)	1.83 (0 – 3.15)	4.0 (0 – 6)
	P < 0.001	P < 0.005	P < 0.005
SA (minor surgery)	4.0 (0 – 20)	1.25 (1 – 5)	2.0 (1 – 8)
SB (medium scale surgery)	8.0 (0 – 38)	2.83 (0.5 – 6)	4.0 (1 – 10)
SC (major surgery)	17.0 (7 – 68)	3.01 (0 – 9)	6.0 (0 – 10)
	P < 0.001	P < 0.1 (n.s.)	P < 0.005

CACS values and corresponding **NRS** values for pain (mean, peak) for different types of urological (yellow field; group **UA =** minor, group **UB =** medium, group **UC =** major) and surgical interventions (red field; group **SA** = minor; group **SB =** medium; group **SC =** major) , levels of significance concerning the ability to differentiate surgical groups (using Kruskal-Wallis-test)

Table 2 - Correlation between CACS and peak NRS.

6 x n = 20 patients	Spearman's rank correlation coefficient	Significance (2-sid.)
UA	0.749	p < 0.001
UB	0.761	p < 0.001
UC	0.303	p = 0.21 (n.s.)
SA	0.797	p < 0.001
SB	0.901	p < 0.001
SC	0.226	p = 0.34 (n.s.)

Correlation between **CACS** and peak **NRS** for pain for different types of surgical and urological interventions (groups **SA/ UA =** minor surgery; groups **SB/ UB =** medium scale surgery; groups **SC/UC =** major surgery)

(AC) and invasiveness of different urological and surgical procedures than NRS pain scores.

In recent years, considerable efforts have been made to further minimize surgical trauma and reduce the adverse effects of surgery. Methods to determine the impact of different surgical approaches such as laparoscopic and open surgery include inflammatory and immunologic markers of invasiveness (5); clinical outcome parameters such as hematocrit drop, duration of surgery and postoperative pain (3,19); and social indicators like time of return to work and to full physical activity (20).

Postoperative pain correlates with the severity of impairment of bodily integrity, and hence with the invasiveness of surgical interventions, with a major impact on surgical site physiological function (21,22) and the patient's functional recovery (23).

However, numerous confounding factors influence the sensation of pain and there is no agreement regarding the best method of assessing pain scores, particularly regarding the timing and frequency of scoring, e.g., prescheduled determination of pain scores (three times a day), recording of peak pain levels, or the temporal context of administration and type of pain medication (9). Others have highlighted the distinction between "pain at rest" (PAR) and "movement-evoked pain" (MEP) and suggested that both PAR and MEP should be measured in postsurgical pain research (24).

In contrast, AC is a CRO (rather than a PRO) and can therefore be used as a surrogate parameter for postsurgical pain (2) and hence for surgical invasiveness. The CACS depicts AC as a non-invasive parameter, unlike the laboratory markers mentioned above.

There is a wealth of literature on AC as a method for measuring the analgesic efficacy of new drugs and other treatment modalities such as nerve blocks and transcutaneous electrical nerve stimulation, and for confirmation of new concepts such as pre-emptive analgesia (more than 600 trials have been performed) (10). However, postsurgical AC has been measured only rarely as a secondary outcome parameter in clinical trials and literature on this topic is scarce. Only one RCT on urolithiasis (25) described AC, stating whether "oral pain medication was used" and the mean duration of use (in days). In other fields, postoperative AC has been assessed as the cumulative dose of a specific drug (e.g., overall tramadole consumption in milligrams) (15,26-28). In a systematic review on predictors of postoperative pain and AC (2), Ip et al. identified a total of 42 studies from different surgical fields. All studies described pain intensity using a VAS or an NRS. Twenty-two other studies also commented on AC, with all describing cumulative doses of one specific drug or computed morphine equivalents. Others used a 5- or 7-point scale to discriminate between the efficacies of different analgesic drugs in the management of bone pain

(29,30). These scales were used over a treatment period of several months to evaluate the effect of bisphosphonates on pain reduction using the mean change from baseline to final assessment. Only one study describing an "analgesic score computed as a product of analgesic type and frequency of administration", could be identified, which had apparently been developed but not validated or published by the authors (31).

However, the use of both pain scores and analgesic consumption scores can be associated with significant potential problems. Indeed, numerous confounding factors influence the sensation of pain and the demand for medication, and therefore AC; these include individual sensitivity to pain medication, interference of non-analgesic effects, and patient and physician attitudes and behaviors, among others (2). An attempt has been made to overcome the covariation between pain intensity, AC and adverse drug effects by using a composite measure that combines pain intensity ratings and rescue medication use into a single score (9). However, this "integrated assessment" was proposed for use in studies of analgesic efficacy and does not seem to be an appropriate tool for assessing the postoperative course in clinical studies, because of its disproportion.

In addition to these inherent problems concerning pain scores and AC, there are additional methodological difficulties. Categorizing and quantifying the effects of different analgesic drugs can result in somewhat constructive vagueness. However, we found that the WHO pain relief ladder (16,17) simplified the potency-related classification of analgesic medication.

The WHO pain relief ladder was primarily conceived for use in the management of cancer pain relief, but is also used for the management of various other types of pain, e.g., postoperative analgesia. Because all types of drugs are to be considered, individual doses in milligrams cannot be calculated. However, assuming that single or combined administrations of analgesic drugs of the respective WHO categories are given at adequate doses (specified baseline or on demand medication), we hypothesized that the quantity (the overall dose of analgesic drugs) could be roughly estimated by counting single administrations of each drug during the pre-defined timeframe, and that the computed product of the frequency of "adequate" administrated single doses and the potency factor (WHO I – III) therefore could serve as a semi-quantitative assessment of overall AC.

The current study suggests a stronger correlation between CACS values and invasiveness of surgical procedures as compared to pain scores. It could be assumed that these findings reflect adequate analgesic therapy. This particularly applies to patients who undergo more invasive procedures; in these patients, good pain control will lead to lower pain scores in spite of higher invasiveness. This is consistent with our finding that correlation between CACS and mean and peak NRS values was significant in patients with minor or medium scale surgery but not in those who had major surgery. These data suggest that the CACS is a superior surrogate parameter to pain scores alone for measurement of the invasiveness of and pain after surgical procedures.

It is of note that in the setting of a specific study that will use CACS an appropriate time frame has to be defined in the study protocol (e.g. 2 days when comparing shock wave lithotripsy and ureteroscopy for stone therapy or 7 days when comparing laparoscopy and open surgery for prostate cancer).

Here, we intended to develop an easy-to-use score that could be applied in everyday clinical practice (e.g., if used as a secondary outcome parameter in clinical studies without specified analgesic regimens). Therefore, all available analgesic drugs had to be categorized using a simple system; the WHO pain relief ladder is a well-known and easily handled tool that can be used for this purpose.

This study had some limitations. The data where acquired retrospectively and the study included a rather small number of patients. However, taking into account that to date most clinical studies are of retrospective design, it may be assumed that the new score will most likely be applied in such a setting. In addition, for reasons described above, global scores are somewhat inaccurate. Furthermore, adjuvant medications (e.g.,

antidepressants, steroids) cannot be included in the CACS. PCA and other types of analgesic treatments, such as postoperative epidural analgesia, can be included in the score but were not considered in this study. It may be argued that patients on analgesic long-term medication will confound results of future clinical trials using CACS. This may be avoided by a prospective randomized design of high impact studies.

We believe that AC should be recorded as a clinical parameter to further describe patients' well-being after interventional or surgical therapies. Pain scores (as PROs) should be supplemented by related CROs (such as AC). The CACS can be used by clinical scientists to compare different surgical and interventional therapies (and even medical/oncological treatments) with respect to AC as a surrogate parameter for pain and invasiveness (surgical) or treatment success (medical/ oncological).

In summary, the CACS can be used to describe AC in many different clinical settings. It provides a semi-quantitative assessment of overall AC within a defined period of time, and as such can be used as a surrogate parameter for pain and the invasiveness of surgical procedures. Expressing AC as a figure on an open-ended scale will provide easy-to-use information to clinical scientists and treating physicians.

ABBREVIATIONS

AC = analgesic consumption
CACS = cumulative analgesic consumption score
CRO = clinically reported outcomes
NRS = numeric rating scale
PCA = patient-controlled analgesia
PRO = patient-reported outcomes
SA = surgical patients from group A
SB = surgical patients from group B
SC = surgical patients from group C
UA = urological patients from group A
UB = urological patients from group B
UC = urological patients from group C
VAS = visual analog scale

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Greco F, Hoda MR, Wagner S, Reichelt O, Inferrera A, Fischer K, et al.: Adipocytokine: a new family of inflammatory and immunologic markers of invasiveness in major urologic surgery. Eur Urol. 2010; 58: 781-7.
2. Ip HY, Abrishami A, Peng PW, Wong J, Chung F: Predictors of postoperative pain and analgesic consumption: a qualitative systematic review. Anesthesiology. 2009; 111: 657-77.
3. Mutoh M, Takeyama K, Nishiyama N, Kunishima Y, Matsukawa M, Takahashi S, et al.: Systemic inflammatory response syndrome in open versus laparoscopic adrenalectomy. Urology. 2004; 64: 422-5.
4. Tenti G, Hauri D: Pain and its treatment in urology. Urol Int. 2004; 73: 97-109.
5. Li LY, Gao X, Yang M, Li JF, Zhang HB, Xu WF, et al.: Does a smaller tract in percutaneous nephrolithotomy contribute to less invasiveness? A prospective comparative study. Urology. 2010; 75: 56-61.
6. Hartrick CT, Kovan JP, Shapiro S: The numeric rating scale for clinical pain measurement: a ratio measure? Pain Pract. 2003; 3: 310-6.
7. Jensen MP, Karoly P, Braver S: The measurement of clinical pain intensity: a comparison of six methods. Pain. 1986; 27: 117-26.
8. Soomro KQ, Nasir AR, Ather MH: Impact of patient's self-viewing of flexible cystoscopy on pain using a visual analog scale in a randomized controlled trial. Urology. 2011; 77: 21-3.
9. Silverman DG, O'Connor TZ, Brull SJ: Integrated assessment of pain scores and rescue morphine use during studies of analgesic efficacy. Anesth Analg. 1993; 77: 168-70.
10. Kissin I: Patient-controlled-analgesia analgesimetry and its problems. Anesth Analg. 2009; 108: 1945-9.
11. McQuay HJ, Poon KH, Derry S, Moore RA: Acute pain: combination treatments and how we measure their efficacy. Br J Anaesth. 2008; 101: 69-76.
12. Essving P, Axelsson K, Kjellberg J, Wallgren O, Gupta A, Lundin A: Reduced morphine consumption and pain intensity with local infiltration analgesia (LIA) following total knee arthroplasty. Acta Orthop. 2010; 81: 354-60.
13. Zhou H, Xu H, Zhang J, Wang W, Wang Y, Hu Z: Combination of dexamethasone and tropisetron before thyroidectomy to alleviate postoperative nausea, vomiting, and pain: randomized controlled trial. World J Surg. 2012; 36: 1217-24.
14. Bazzi WM, Stroup SP, Kopp RP, Cohen SA, Sakamoto K, Derweesh IH: Comparison of laparoendoscopic single-site and multiport laparoscopic radical and partial nephrectomy: a prospective, nonrandomized study. Urology. 2012; 80: 1039-45.

15. Gagliese L, Gauthier LR, Macpherson AK, Jovellanos M, Chan VW: Correlates of postoperative pain and intravenous patient-controlled analgesia use in younger and older surgical patients. Pain Med. 2008; 9: 299-314.
16. Organisation WH (1996) Pain - Drug therapy. Cancer Pain Relief. With a guide to opioid availability. WHO Press. Available at: http://whqlibdoc.who.int/publications/9241544821.pdf
17. Stjernswärd J, Colleau SM, Ventafridda V: The World Health Organization Cancer Pain and Palliative Care Program. Past, present, and future. J Pain Symptom Manage. 1996; 12: 65-72.
18. Porena M, Guiggi P, Balestra A, Micheli C: Pain killers and antibacterial therapy for kidney colic and stones. Urol Int. 2004; 72(Suppl 1): 34-9.
19. Bryniarski P, Paradysz A, Zyczkowski M, Kupilas A, Nowakowski K, Bogacki R: A randomized controlled study to analyze the safety and efficacy of percutaneous nephrolithotripsy and retrograde intrarenal surgery in the management of renal stones more than 2 cm in diameter. J Endourol. 2012; 26: 52-7.
20. Majeed AW, Troy G, Nicholl JP, Smythe A, Reed MW, Stoddard CJ, et al.: Randomised, prospective, single-blind comparison of laparoscopic versus small-incision cholecystectomy. Lancet. 1996; 347: 989-94.
21. Vassilakopoulos T, Mastora Z, Katsaounou P, Doukas G, Klimopoulos S, Roussos C, et al.: Contribution of pain to inspiratory muscle dysfunction after upper abdominal surgery: A randomized controlled trial. Am J Respir Crit Care Med. 2000; 161: 1372-5.
22. Wess OJ: Chronic pain and pain relief by extracorporeal shock wave therapy. Urol Res. 2011; 39: 515-9.
23. Wu CL, Rowlingson AJ, Partin AW, Kalish MA, Courpas GE, Walsh PC, et al.: Correlation of postoperative pain to quality of recovery in the immediate postoperative period. Reg Anesth Pain Med. 2005; 30: 516-22.
24. Srikandarajah S, Gilron I: Systematic review of movement-evoked pain versus pain at rest in postsurgical clinical trials and meta-analyses: a fundamental distinction requiring standardized measurement. Pain. 2011; 152: 1734-9.
25. Pearle MS, Nadler R, Bercowsky E, Chen C, Dunn M, Figenshau RS, et al.: Prospective randomized trial comparing shock wave lithotripsy and ureteroscopy for management of distal ureteral calculi. J Urol. 2001; 166: 1255-60.
26. Cepeda MS, Carr DB: Women experience more pain and require more morphine than men to achieve a similar degree of analgesia. Anesth Analg. 2003; 97: 1464-8.
27. Katz J, Buis T, Cohen L: Locked out and still knocking: predictors of excessive demands for postoperative intravenous patient-controlled analgesia. Can J Anaesth. 2008; 55: 88-99.
28. Remzi M, Klingler HC, Tinzl MV, Fong YK, Lodde M, Kiss B, et al.: Morbidity of laparoscopic extraperitoneal versus transperitoneal radical prostatectomy verus open retropubic radical prostatectomy. Eur Urol. 2005; 48: 83-9; discussion 89.
29. Body JJ, Diel IJ, Bell R, Pecherstorfer M, Lichinitser MR, Lazarev AF, et al.: Oral ibandronate improves bone pain and preserves quality of life in patients with skeletal metastases due to breast cancer. Pain. 2004 ; 111: 306-12.
30. Kristensen B, Ejlertsen B, Groenvold M, Hein S, Loft H, Mouridsen HT: Oral clodronate in breast cancer patients with bone metastases: a randomized study. J Intern Med. 1999; 246: 67-74.
31. Tripathi M, Singhal T, Chandrasekhar N, Kumar P, Bal C, Jhulka PK, et al.: Samarium-153 ethylenediamine tetramethylene phosphonate therapy for bone pain palliation in skeletal metastases. Indian J Cancer. 2006; 43: 86-92.

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