Original Article

Evaluation of transversus abdominis plane block for renal transplant recipients – A meta-analysis and trial sequential analysis of published studies

ABSTRACT

Background: Patients undergoing renal transplant (RT) have altered drug/opioid pharmacokinetics. Transversus abdominis plane (TAP) block in renal transplant recipients has been recently evaluated for analgesic and opioid-sparing potential by many trials.

Methodology: The studies comparing TAP-block to conventional analgesic regimens for RT were searched. Comparisons were made for total opioids consumed (as morphine-equivalents) during the first postoperative 24-h (primary objective), intraoperative, and immediate-postoperative period. Pain scores and postoperative nausea-vomiting (PONV) were also evaluated. Trial sequential analysis (TSA) was used to quantify the strength of analysis.

Results: Ten-trials with 258 and 237 patients in control and TAP-block group, respectively, were included. TAP-block decreased the 24-h (reported in 9-trials) opioid consumption by 14.61 ± 4.34 mg (reduction by 42.7%, random-effects, $P < 0.001$, $I^2 = 97.82\%$). Sample size of the present analysis (472) was well past the required "information-size" variable (396) as per the TSA for a power of 85%. Intraoperative opioid consumption also decreased by 2.06 ± 0.63 mg (reduction of 27.8%) (random effects, $P < 0.001$, $I^2 = 98.84\%$). Pain scores with TAP-block were significantly lower in both early and delayed postoperative phase. Odds ratio for PONV without TAP block was 1.99 ± 1.05 (Fixed-effects, $P = 0.04$, $I^2 = 0\%$). Publication bias was likely (Egger's test, X-intercept=7.89, $P < 0.05$).

Conclusions: TAP-block significantly lowers the intraoperative and cumulative postoperative 24-h opioid consumption in RT recipients. Persistent and better pain control is achieved when TAP-Block is used. Benefits of TAP block extend beyond the analgesic actions alone as it also decreases the 24-h incidence of postoperative nausea vomiting as well. The technique of the block needs standardization for RT recipients.

Key words: Renal recipients analgesia; transplant recipients; transversus abdominis plane block

Introduction

Postoperative analgesia for patients undergoing renal transplant is a major challenge for the transplant teams.

Prescription of analgesics requires considerations for altered pharmacological profile of the drugs and possibly

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higher incidence of associated adverse reactions. A major limitation in providing optimal multimodal analgesia in these patients is the contraindication of the use of renotoxic nonsteroidal anti-inflamatory drugs (NSAIDs). NSAIDs are known to adversely affect the glomerular filtration rate, and thus need to be avoided in patients receiving graft kidney. Thus, in the absence of one of the frontline analgesic drug class (NSAIDs), perioperative care team has to rely heavily on the use of opioids or different forms of regional analgesia. Epidural analgesia, which is a well-accepted gold standard for major abdominal surgeries also has limitations in this population. Ample literature is available suggesting against the use of central neuraxial block in patients with chronic renal failure in view of associated platelet functional disorders that may predispose them to epidural hematoma formation.[1-3]

Globally, multiple trials have evaluated regimens that can provide opioid-sparing analgesia for patients undergoing organ transplant. The advent of ultrasound-guided regional anesthesia has paved the way for newer and safer blocks in patients undergoing open abdominal surgeries. Transversus abdominis plane (TAP) is one such option that has emerged for renal transplant recipients. Recently, many studies have evaluated TAP block's efficacy for perioperative analgesia and opioid-sparing potential in renal transplant recipients. The results from a few trails have failed to demonstrate clear benefits, whereas on the contrary, others have reported significantly better analgesic efficacy in comparison to the conventional analgesic regimens. The studies have reported the inability of TAP block to provide analgesia for the visceral pain component and thus question its analgesic potential/utility. We undertook this meta-analysis to consolidate the available evidence and to quantify the analgesic potential/opioid sparing capability of TAP block in patients undergoing renal transplant surgery.

Methodology

Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines were followed for the present analysis [Figure 1]. Further, we used a population, intervention, control, and outcome study (PICOS) format for the identification of the potential trials that could be included in the present meta-analysis. After literature search, trials were abstracted into a standardized PICOS format [Table 1] and relevance to our present study question was assessed by two independent reviewers (PMS and AB). The studies evaluating the comparative cumulative doses of opioids (morphine equivalents) during perioperative period in patients undergoing renal transplant surgery (recipients) were

included as the primary outcome in the analysis. After the search, we also planned to compare other parameters (those were consistently reported across different trials) as our secondary/explorative objective. The salient features of trials included in the final analysis that met the above criterion are shown in Table 2.

Search strategy

The preliminary data search was performed by two independent researchers in the following medical database – Science Citation Index Expanded, Embase, Scopus, Cochrane Central Register of Controlled Trials, clinical trials registry, google scholar, Pubmed, and meta-register of controlled for published manuscripts. Comparative trials published until April 2, 2017 were included in the analysis. The following medical subject heading terms were searched for in the above-said database – Perioperative transplant analgesia, renal recipient regional anesthesia, transversus abdominis plane block renal transplant, and TAP block opioid sparing renal transplant. We excluded the following terms from the search string-TAP block in renal donor, epidural analgesia renal transplant, and renal donor analgesia. We reviewed/included comparative trials of both prospective and retrospective nature in this analysis.

To evaluate the efficacy of TAP block alone, we avoided trials that used additional nerve blocks in combination with TAP block (epidural, quadratus lumborum, ilioinguinal

Table 1: Population, intervention, control, and outcome study data extraction framework

	PICOS Framework
Population	Adult patients with known chronic renal failure undergoing renal transplant surgery (Recipients).
Interventions	Patients receiving local anesthetic based transverse abdominis plane (TAP) block during the preoperative or immediately after the surgery. The TAP block could be single shot or catheter guided continuous block. TAP block could be ultrasound guided, tactile pop based or surgeon assisted catheter insertion during closure Receiving multimodal intravenous rescue analgesia
Controls	Renal recipients undergoing transplant surgery and receiving perioperative multimodal intravenous analgesia (paracetamol + opioids)

Outcomes	Primary outcomes
	  Comparison of first postoperative day opioids (in morphine equivalents) consumption in both the groups
	Secondary outcomes
	  Intraoperative opioids consumption (where TAP block was given preoperatively)
	  Post-anesthesia care unit (PACU) opioid consumption (during early postoperative phase- first 6 h after surgery)
	  First postoperative day - postoperative nausea vomiting incidence comparison

Study design	Comparative trials evaluating use of TAP block against conventional intravenous analgesics - including prospective, retrospective cohort and case note series.
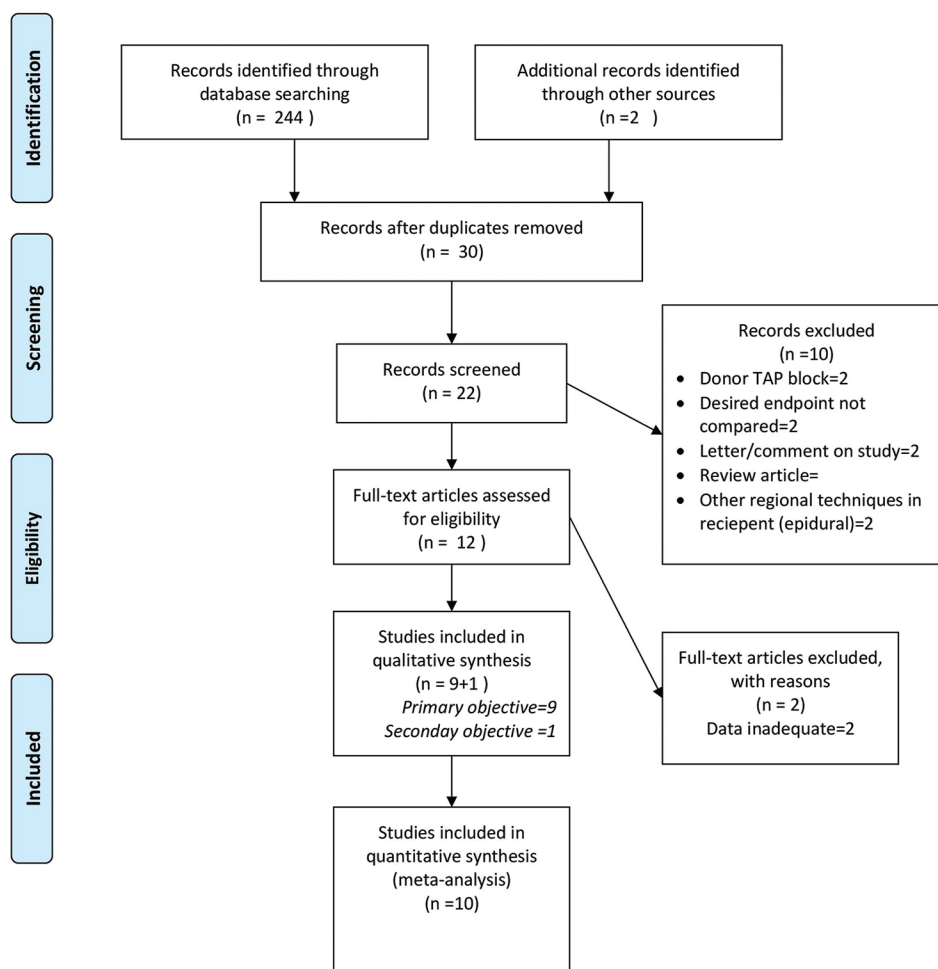
Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram illustrating flow chart outlining retrieved, excluded, and included studies

block, etc.). Our search extended to research articles published either as full manuscripts or meeting abstracts in peer-reviewed journals. We also manually searched the references of comparable meta-analysis for relevant trials. Peer-reviewed abstracts published in the proceedings of meetings were also screened. Our search included trials published in both English and non-English languages. Once the abstract was analyzed by the searching reviewer and found appropriate, the full text of the article was further studied. The decision to include a trial into final analysis was based on the independent assessment of the two independent reviewers. Any disagreements between the two were harmonized by consensus and arbitration by a third neutral reviewer. Based on the recommendations framed by the Cochrane Collaboration, another independent researcher assessed the included trials for quality of evidence and possible methodological bias.

Data extraction

Data were abstracted into a standardized format entered into Microsoft Excel 2016 (Microsoft Corporation, USA). The following data from individual studies was extracted: Study design, year and country of publication, participant numbers primary/secondary outcome reported, drug, volume and concentration used in TAP block, use of ultrasound-guided block, use of catheter for continuous block, analgesia methods in control group, opioids used in perioperative period, numeric pain scores at various time points, incidence of postoperative nausea vomiting, and specific adverse effect (if mentioned) [Table 2]. If data was expressed in terms of median and interquartile range, the authors were contacted for the mean and standard deviation (SD) values. However, if authors did not reply, as a last resort we estimated the mean using the validated formula: Mean $= 2m + a + b/4$ where m is the median and

Table 2: Included studies characteristics

Author/year	Country	Study design	Number of groups	USG guided TAP	TAP catheter	IV opioid used	Local anesthetic in TAP	Volume of local anesthetic (ml)	Measured outcomes
Abdelsalam and Sultan, 2015[4]	Cairo, Egypt	RCT-blinded	2 TAP/IV	Yes	No	Intraoperative fentanyl Postoperative morphine	0.5% bupivacaine	20	Intraoperative opioid PACU opioid 24-h opioid PONV
Mukhtar and Khattak, 2010[5]	Liverpool, United Kingdom	Retrospective cohort	2 TAP/IV	No	No	Intraoperative morphine Postoperative morphine	0.5% bupivacaine	20	Intraoperative opioid 24-h opioid PONV (no values given) Sedation (no values given)
Farag et al., 2015[6]	Ohio, USA	Retrospective review-case note analysis	2 TAP/IV	Yes	Yes	Intraoperative-oral morphine equivalents reported	0.5% ropivacaine	20	Intraoperative opioid 48-h cumulative opioids
Freir et al., 2012[7]	Dublin, Ireland	RCT-blinded	2 TAP/IV	No	No	Intraoperative morphine Postoperative morphine	0.375% levo-bupivacaine	20	Intraoperative opioid PACU opioid 24-h opioid PONV
Jankovic et al., 2009[8]	Leeds, United Kingdom	Retrospective review-case note analysis	2 TAP/IV	Yes	Yes Surgically placed-before closure	Postoperative morphine (PCA)	0.375% Levobupivacaine	20	Intraoperative opioid 24-h opioid
Soltani Mohammadi et al., 2014[9]	Tehran, Iran	RCT-blinded	2 TAP/IV	Yes	No	Intraoperative fentanyl Postoperative morphine (PCA)	0.25% bupivacaine	15	Intraoperative opioid 24-h opioid PONV NRS pain scores-up to 24 h
Parikh et al., 2015[10]	Gujrat, India	RCT-blinded	2 TAP/IV	No	Yes	Postoperative pentazocine	0.125% bupivacaine	Postoperative infusion only	24-h opioid NRS pain scores-up to 24-h Sedation scores
Afridi et al., 2015[11]	Tyne and Wear, United Kingdom (Conference abstract only)	Prospective nonrandomized	2 TAP/IV	No	No	Postoperative fentanyl (PCA)	Details not available	Details not available	Intraoperative opioid PACU opioid 24-h opioid PONV
Gopwani and Rosenblatt, 2016[12]	Washington, USA	Retrospective review-case note analysis	2 TAP/IV	Yes	No	Intraoperative fentanyl Postoperative morphine	0.25% bupivacaine	20	PACU opioid 24-h opioid 48-h opioid
Gulyam et al., 2014[13]	Warrington, United Kingdom	RCT-blinded	2 TAP/TAP placebo	Yes	No	Intraoperative fentanyl Postoperative morphine (PCA)	0.25% bupivacaine or 0.25% ropivacaine	20	24-h opioid NRS pain scores-up to 24-h Sedation scores nausea score (no details available only P value given)

RCT: Randomized controlled trial; TAP: Transverse abdominis plane block; IV: Intravenous; USG: Ultrasound guided; PACU: Postanesthesia care unit; PONV: Postoperative nausea-vomiting; PCA: Patient-controlled analgesia; NRS: Numeric rating scale (for pain)

a and b are the 25th and 75th centiles, respectively.[14] The SD was estimated by the formula given by the Cochrane collaboration: interquartile range = 1.35 SD.[15,16] The pain scores wherever documented were converted to a common denominator scale of 0–10 using unitary method where "0" meant no pain and "10" denoted worst possible pain. Adobe Illustrator (Adobe Systems Inc., USA) was used to convert graphical data presented in the studies into vector images. This allowed us to obtain numeric values of the pain scores where they were presented only as graphs.

Statistical analysis

The statistical analysis of the pooled data was performed using Comprehensive Meta-Analysis-Version 3 (Biostat Inc., USA). Meta-analysis was performed using fixed effect modeling and eventually with random-effect methods (after the assessment of heterogeneity with fixed modeling). I^2 statistic was used to quantify the heterogeneity between the trials. Values of $I^2 < 40\%$ were considered nonsignificant, 40%–60% were considered to represent moderate heterogeneity, 60%–90% was deemed as high heterogeneity. Comparative results were expressed as pooled mean difference for continuous variables and Mantel–Haenszel (MH) odds ratio for dichotomous variables. $P < 0.05$ was considered statistically significant. Wherever, heterogeneity was found to be lower than 40% results from "fixed effect modeling" are used else results from random effect modeling are presented. Potential publication bias quantified using the Egger's regression test, and it was further evaluated using the funnel plot. To determine the appropriate sample size for the meta-analysis, we performed a "trial sequential analysis" (TSA) using the TSA Module (Copenhagen trial unit, Denmark). For the TSA modeling, estimates of information size (IS) variable were made allowing a beta error of 0.15.

Results

Preliminary search identified 244 articles from the abovementioned database. Duplicates obtained from individual search by different reviewers were identified and were removed using Endnote (Thompson Reuters, USA). Eventually, seven trials were identified that measured/reported the primary outcome or the secondary outcomes. One additional trial by Afridi *et al.*[11] (published as a meeting abstract after peer review-based acceptance in "2015 American Transplant Congress") also reported desired outcomes and was identified through Google scholar. Thus,

a total of 8 trials were included in the final analysis. Two of these (trials by Mukhtar and Khattak and Jankovic *et al.*)[5,8] were published as research communications/letters and both were reported to be peer reviewed before publication (as per the published journal policy). Opioid doses/requirements for all included trials were converted into intravenous morphine equivalents before computation. For this conversion, we used the validated opioid conversion table available in the literature.[17]

Six trials [Table 2] reported the use of ultrasound-guided TAP block and the rest used either blind- or surgeon-assisted TAP block (at the end of surgery before the closure). Initial bolus of 20 ml of 0.25% bupivacaine was the most popular choice to initiate the TAP block and was used in 4 trials. Two trials used 20 ml of 0.375% levobupivacaine and one trial used 20 ml of 0.125% bupivacaine [Table 2]. Trial by Afridi *et al.* did not document the drug used and only referred to as local anesthetic. Only two trials threaded a catheter in the transversus abdominis plane and used local anesthetic infusion for the postoperative phase.

Block-related adverse effects were not consistently documented/compared across the trials and thus no statistical comparisons could be made. Four trials, however, compared the incidence of postoperative nausea vomiting between TAP block and control group. Thus, we were able add comparison of PONV as our explorative objective.

Intravenous morphine equivalent doses could be calculated for the following time points.

Postoperative day one [Figure 2]

Data for this comparison were available in 9 trials that included 290 patients in control and 243 patients in the TAP block group. Patients receiving single shot or continuous TAP
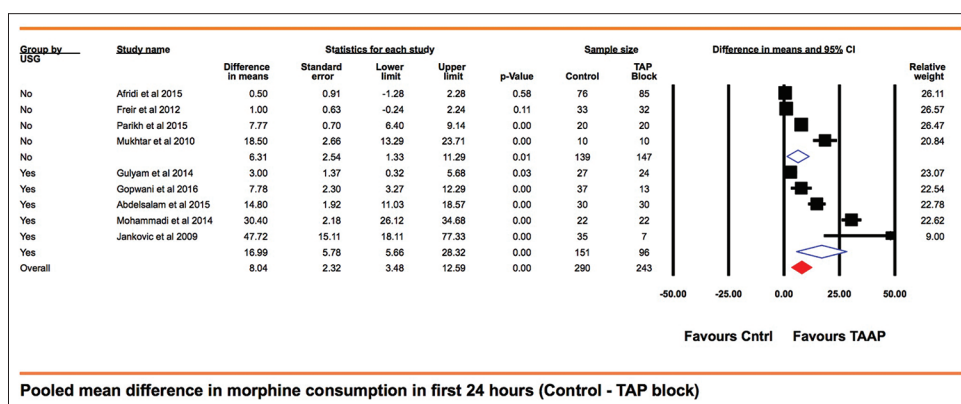

Figure 2: Forest plot showing pooled mean difference for first postoperative 24-h opioid consumption in morphine equivalents (control group-transversus abdominis plane block group). Subtypes within type of transversus abdominis plane block are shown separately with their summary represented by the empty diamond in the graph. Solid diamond at the bottom of comparison denotes the final net effect

block showed significantly lower morphine requirements in the first 24 h after the surgery. Overall, TAP block showed a morphine-sparing effect with 14.79 (95% confidence interval [CI] being 3.48–12.59) mg use of morphine. The mean morphine consumption in the control group was 29.4 mg, and this reduction meant a reduction was nearly 42.7% of the total opioid consumption. The heterogeneity for this comparison was 97.82% [Figure 2]. To explore the heterogeneity, we performed a subgroup analysis subdividing the block group into "single shot" and "continuous TAP block." Single shot group (5 trials) was also statistically significantly better than control group (two trials) ($P < 0.001$) with $I^2 = 95.48\%$. Although both the individual trials in the continuous group showed statistically significantly lower morphine consumption, pooled difference failed to attain the desired statistical significance ($P = 0.21$). This was deemed because of small sample size in this subgroup. All these nine studies reporting the primary outcome were also further subgrouped based on the use of ultrasound for TAP block. Four studies reported to have used blind technique (landmark based) and five used ultrasound-guided TAP block. Pooled mean morphine consumed with blind TAP block was lower by 6.31 mg (95% CI being 1.33–11.26) compared to control group ($P = 0.013$, $I^2 = 96.86\%$). For trials using ultrasound-guided TAP, the pooled mean reduction was significantly higher being 26.41 mg (95% CI being 12.06–40.67) ($P < 0.001$, $I^2 = 93.70$). For ultrasound-guided TAP block, subgroup results need to be interpreted cautiously because of high contribution from the study by Jankovic *et al.* (relative weight being 15.29%). Data from this study appear to be significantly skewed, and thus, the authors presented their results in form of median and range. It must, however, be noted that in the overall results (total morphine consumed), the "proportional weight" of Jankovic *et al.* was much smaller (weight = 3.50%) and thus the contributed skew effect is negligible. Exploring for heterogeneity using "single study removal method" showed that nearly all studies contributed equally toward the pooled heterogeneity highlighting the possibility of large interstudy methodological differences.

Trial sequential analysis
To validate the overall findings and adequacy of the sample size of the present meta-analysis, a TSA was performed. This analysis was performed for mean difference 24-h morphine consumption between the two groups using two different significance testing methods. The conventional boundary (with alpha error of 5% as limit) and the alpha-spending boundary (Upper O'Brien Fleming with type 1 error of 5%). For determining the "IS" variable, the power was set at 85%. IS was determined to be by alpha-spending boundary method. The actual number of patient's in our

analysis was higher being 533 (290 + 243), thus IS for analysis was adequate. The cumulative "Z score" limit was found to be well past the limits by either of the above analyzing method [Figure 3]. Thus, the possibility of a false-positive result in the present meta-analysis is ruled out.

Intraoperative consumption
Values were available for 7 trials for this variable. Parikh *et al.* used a catheter for TAP block activating it during the postoperative phase, and thus, intraoperative values for morphine consumption were not compared. The mean morphine consumption in patients receiving local anesthetic-based TAP block was lower by 1.74 (95% CI being 0.62–2.86) mg. The heterogeneity for this comparison was high being 98.84% [Figure 4]. We used a sensitivity analysis using the "single study removal method" to explore the high heterogeneity. Trial by Farag *et al.* contributed the highest toward the total heterogeneity and its removal dropped the heterogeneity to 74.73%.

Immediate postanesthesia care unit phase
Opioid consumption during the first 6 h in the immediate postoperative phase was compared for both the groups. Although the trend toward lower morphine consumption was noted [Figure 5], due to small sample size (only 5 studies), the pooled value failed to attain a statistical significance ($P = 0.09$, $I^2 = 97.34\%$).

Postoperative pain scores
Pain scores reported (on a scale of 0–10) were analyzed for two time points in the postoperative phase.

Immediate postanesthesia care unit pain scores
Scores reported by trials within first 6 h of surgery were pooled. Five trials quantified the comparative pain scores during this period. The pooled mean pain scores were lower by 1.47 (95% CI being 0.21-2.72) in the TAP block group ($P = 0.02$). This comparison suffered a high heterogeneity (99.05%) [Figure 6].

Postoperative day one pain scores
Five trials reported pain scores at the end of first 24 h after surgery. Pooled mean scores were lower by 0.68 (95% CI being 0.06–1.3). The heterogeneity for this comparison was 98.36% with a $P = 0.03$ [Figure 7].

Postoperative nausea vomiting
Four trials reported the number of patients with PONV during the first 24 h after the surgery. The pooled incidence of PONV in TAP block and control group was 11.2 (95% CI being 7.32–16.89)% and 19.88 (95% CI being 14.45–26.71)%, respectively. The MH-Odds ratio for PONV in patients without TAP block was significantly higher being 1.99 (95% CI being
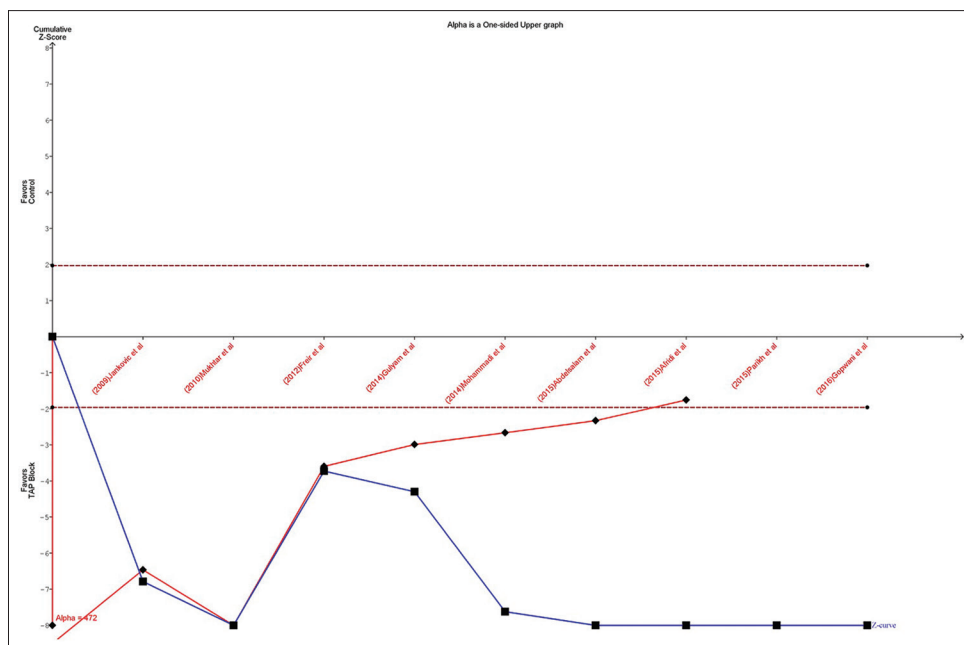
Figure 3: Trial sequential analysis for length of stay. The lower half of the graph below the zero axis falls into the area of advantage with transversus abdominis plane block and the upper half represents the harm area. Solid line (Brown) at -2 on Y-axis represents the conventional model boundaries for trial sequential analysis with an α of 5%. The IS for alpha-spending boundary model = 396 (shown on vertical line along X-axis in red). Cumulative Z scores and the area covered by the Z-score line exceeds the area covered by the sloping solid red line constructed for O'Brien Fleming alpha-spending boundary model (shown by solid red line)
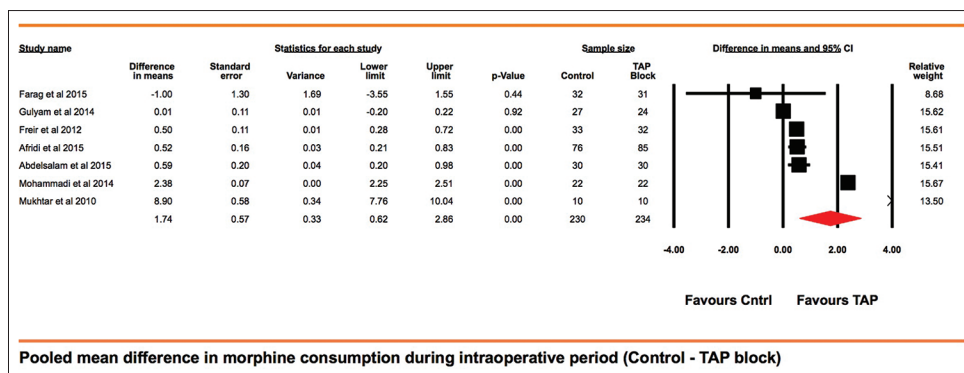

Figure 4: Forest plot showing pooled mean difference for intraoperative opioid consumption in morphine equivalents (control group-transversus abdominis plane block group). Solid diamond at the bottom of comparison denotes the final net effect
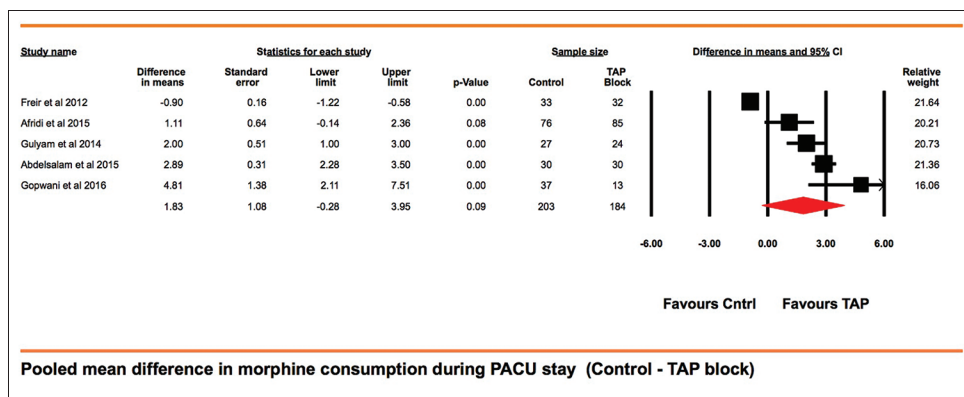

Figure 5: Forest plot showing pooled mean difference for immediate postoperative opioid consumption in morphine equivalents during stay in postanesthesia care unit for until first 6 h after surgery (control group-transversus abdominis plane block group). Solid diamond at the bottom of comparison denotes the final net effect
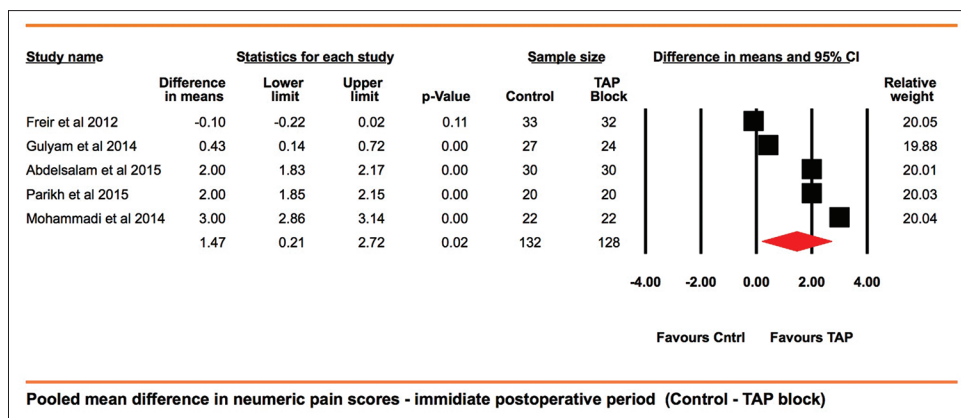
Figure 6: Forest plot showing pooled mean difference in immediate postoperative (within 6 h) numeric pain scores (control group-transversus abdominis plane block group). Solid diamond at the bottom of comparison denotes the final net effect
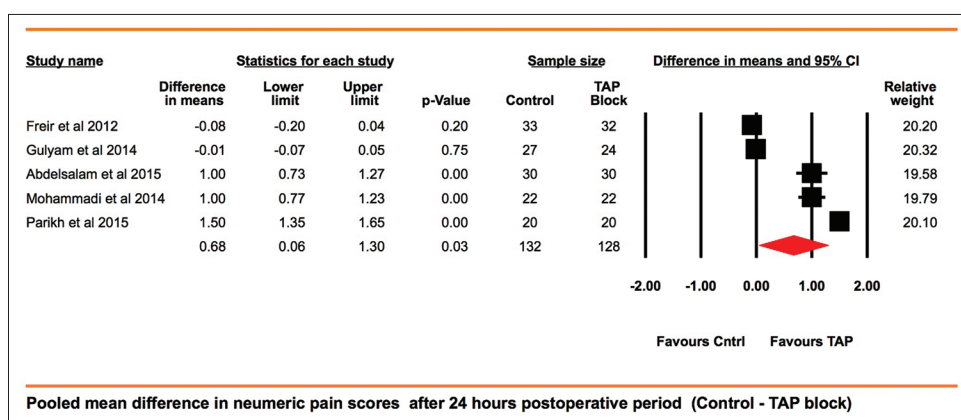

Figure 7: Forest plot showing pooled mean difference in numeric pain scores at the end of first postoperative day (control group-transversus abdominis plane block group). Solid diamond at the bottom of comparison denotes the final net effect
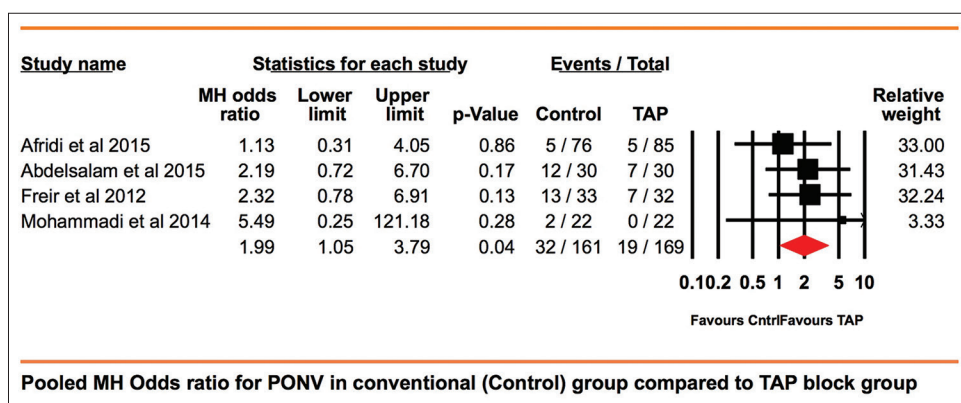

Figure 8: Forest plot showing Mantel-Haenszel-odds ratio for postoperative nausea vomiting during first 24-h postoperatively in patient who did not receive transversus abdominis plane block. Solid diamond at the bottom of comparison denotes the final net effect

1.05–3.79) ($P = 0.04$). The heterogeneity for this comparison was 0% [Figure 8]. Number needed to harm for PONV by omitting perioperative TAP block was estimated to be 15.44.

Publication bias

Publication bias was evaluated for the primary variable. The possibility of publication bias with studies preferentially reporting smaller morphine consumption with TAP block is likely in the presently available literature. Funnel plot distribution was clearly skewed with more study results falling beyond expected neutral funnel boundary (toward positive side) [Figure 9]. Egger's regression test also confirmed the above finding. The X-axis intercept was found at 7.89 with P value (two-tailed) being 0.001.
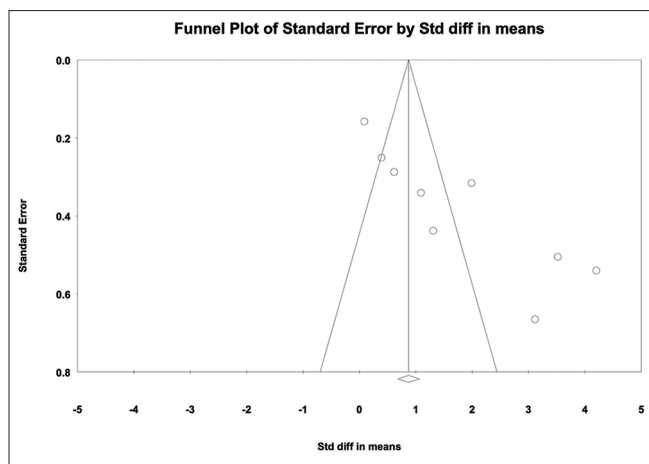
Figure 9: Funnel plot evaluating publication bias length of stay showing asymmetrical distribution of trials. A positive publication bias is expected with X-intercept at + 8.12 with P value being 0.004 (two-tailed)

Study quality assessment

Quality assessment for bias in the included studies was carried out as per other published meta-analysis and the guidelines laid by the Cochrane collaboration. These results are shown in Figure 10. We used Review Manager Version 5.3 (Cochrane collaboration) for this evaluation and image generation.

Discussion

Our meta-analysis demonstrates a significant morphine sparing effect of the TAP block in patients undergoing renal transplant surgery. Despite this smaller opioid consumption, the numeric pain scores were better persistently with TAP block. Patients in the immediate transplant period undergo massive fluid shifts once graft starts to function. On the contrary, unfortunately, if the graft does not function adequately, the fluid dynamics are still unpredictably altered. Under both these circumstances, the pharmacology of systemically administered drugs remain uncertain. As demonstrated by the present analysis, TAP block reduces opioid (morphine equivalent) requirements by nearly 40%, and this is likely to have a positive clinical impact by lowering the need for systemic analgesic drug administration. Needless to say that opioids are known to have more pronounced adverse respiratory and cardiovascular effects, yet this should not lead to under treatment of pain.[18,19] Thus, this reduced drug requirement only adds a margin of safety without undertreating perioperative pain. Persistent lower pain scores in TAP block group (both early and delayed postoperative phase) demonstrate that this increased safety margin (by decreased opioid requirements) is in fact also associated with better pain control. We were also able to demonstrate that ultrasound-guided TAP blocks have higher efficacy in terms

Figure 10: Risk of bias – Summary of all analyzed studies as per the Cochrane collaboration recommendations

of opioid sparing in comparison to blind techniques. Thus, wherever available use of ultrasound should be preferred for performing the block.

Many trials have failed to demonstrate clear evidence in favor of TAP block. Studies by Afridi *et al.* and Freir *et al.* included in the present analysis did not find a conclusive evidence supporting either conventional analgesic regimes or TAP block.[7,11] On the contrary, other included trials reported a statistical/clinical advantage with the use of TAP block. The probable reason underlining these contrasting results originates from the variations in the anatomical location and techniques of TAP block used by different authors. Literature has demonstrated that posterior TAP block due to probable spread to paravertebral space is more effective than the

recent anterior modification.[20,21] Unfortunately, none of the study describes the location of TAP block used by them. In addition, use of ultrasound for TAP block is also not consistent across the trials. In agreement to our analysis, evidence from other abdominal surgeries also suggests that TAP blocks performed by the blind techniques often have lower efficacy in comparison to those performed using ultrasound.[22] Thus, even without considering other methodological variations in the included studies (such as intravenous analgesic regimens) the disparities within the technique of TAP block could have resulted in the high heterogeneity. Further on, the use of continuous local anesthetic infusion in the transversus abdominis plane would have contributed to significant and sustained opioid requirements reduction. The pooled results after subgrouping failed to demonstrate this in catheter group because of only small proportion of studies (only two) used a TAP catheter.

We also found a clear reduction in intraoperative morphine equivalents consumed (by 2.06 mg) in the TAP block group. This amounted to nearly a 33% decrease in opioid consumption in comparison to the control group (mean consumption 6.06 mg). The implication of this result translates into higher likelihood of a clear-headed recovery in patients undergoing transplant. It is a well-known fact that general anesthetics compounded with raised blood urea nitrogen have a more profound sedative effect. Any reduction in intraoperative opioid analgesics (that also cause sedation) would be a step toward a better recovery profile and eventually lower the incidence of sedation-related complications. Both Mukhtar and Khattak and Freir *et al.* (included in our analysis) demonstrated that immediate postoperative sedation scores were in fact lower in patients who received TAP block.[5,7]

In the immediate postoperative phase, we were unable to find any statistically significant opioid sparing with the use of single shot TAP block or catheter-based continuous TAP block. This finding seems contrary to the intuitive thinking as the expected benefits would be rather more in early postoperative phase. The expected half-life of local anesthetic-based TAP block is around 6–8 h.[23] Although a trend toward lower opioid consumption with TAP block was evident, statistical significance for the result could not be attained. Only a small proportion of studies reported this variable (three trials), andthus this has more of a mathematical bearing rather than being a clinical shortcoming of the TAP block. However, we wish to highlight that despite statistically indistinguishable opioid use, pain scores were notably lower with the use of TAP block. Thus, for opioid consumption, more studies are required to make statistically valid conclusions.

Perioperative patient satisfaction toward surgery is influenced by many factors. Pain and postoperative nausea vomiting top the list of causes of dissatisfaction.[24,25] Our analysis shows that not only analgesic requirements in TAP block are lower but also the pain scores and the PONV incidence is also significantly smaller. Many direct and indirect factors could have contributed toward this desirable outcome for PONV. Other than direct relation of opioids consumed, higher pain scores are known to directly increase PONV as well.[26] Supporting this, studies included in our analysis by Soltani Mohammadi *et al.* and Parikh *et al.* demonstrated that overall numeric rating scale (NRS) for pain had significantly lower values with the use of TAP block.[9,10] Patients with chronic renal failure have higher incidence of PONV due to associated azotemia a reduction in PONV incidence is likely to improve overall patient satisfaction in renal transplant recipients.[27]

Limitation

Our results related to the perioperative opioid consumption suffer high heterogeneity. As already discussed reasons could be methodological difference in studies, variations in TAP block (use of ultrasound, use of catheter, difference is time of activation of TAP catheter etc.) We attempted multiple methods to explore for the cause of this heterogeneity. Due to small number of total studies, a meta-regression for individual factors was not possible. Subgroupings were done wherever possible, but we needed at least three or more studies for pooling the results in each subgroup, and this was not possible in all subgroups made. Thus, to validate our findings and evaluate the strength of evidence, we performed trial sequential analysis. TSA demonstrated that "IS" for 24-h morphine consumption was adequate and the power of meta-analysis is more than 85%. The study by Jankovic *et al.* clearly had skewed data for opioid consumption. Thus, they reported values in terms of median and range. For pooling opioid consumption value, "estimated mean" was computed. Although the total weight of this study in the overall pooled result was only 3.50%, it could have marginally effected the results. Another challenge we faced during summarizing our result was the absence of consistent documentation/comparison of adverse events related to the block. This would have helped us to evaluate the safety of the block as well.

Conclusions

Use of TAP block in renal recipients undergoing transplant surgery has high opioid-sparing potential. It significantly lowers the cumulative postoperative 24-h opioid consumption in comparison to the conventional intravenous analgesic regimens. Opioid analgesic requirements during the intraoperative period are also smaller when TAP block is

instituted preoperatively. Better persistent pain control can be achieved throughout the first postoperative day with the use of TAP block. Benefits of TAP block extend beyond the analgesic actions alone as it also decreases the 24-h incidence of postoperative nausea vomiting during renal transplant surgery.

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Conflicts of interest

There are no conflicts of interest.

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