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Three-dimensional virtual planning for nodule resection in solid organs: A systematic review and meta-analysis

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A R T I C L E I N F O

Keywords:
Three-dimensional
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Liver
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A B S T R A C T

Objectives: To systematically review the effects of 3D-imaging virtual planning for nodule resection in the following solid organs: lung, liver, and kidney.
Methods: MEDLINE, EMBASE, and Cochrane Library were searched through September 31, 2020 to include randomized and non-randomized controlled studies that compared outcomes of surgical resection of lung, liver, or kidney nodule resection with and without 3D virtual planning with computed tomography. From each article, the mean operation time (OT), mean estimated blood loss (EBL), mean postoperative hospital stay (POHS), and the number of postoperative events (POE) were extracted. The effect size (ES) of 3D virtual planning vs. non-3D planning was extracted from each study to calculate the pooled measurements for continuous variables (OT, EBL, POHS). Data were pooled using a random-effects model.
Results: The literature search yielded 2397 studies and 10 met the inclusion criteria with a total of 897 patients. There was a significant difference in OT between groups with a moderate ES favoring the 3D group (ES,-0.56; 95%CI: 0.91,-0.29; $I^2 = 83.1\%$; $p < .001$). Regarding EBL, there was a significant difference between 3D and non-3D with a small ES favoring IGS (ES,-0.18; 95%CI: 0.33,-0.02; $I^2 = 22.5\%$; $p = .0236$). There was no difference between the 3D and non-3D groups for both POHS (POHS ES,-0.15; 95%CI: 0.39,0.10; $I^2 = 37.0\%$; $p = .174$) and POE (POE odds ratio (OR),0.80; 95%CI:0.54,1.19; $I^2 = 0.0\%$; $p = .0.973$).
Conclusions: 3D-imaging planning for surgical resection of lung, kidney, and liver nodules could reduce OT and EBL with no effects on immediate POHS and POE. Improvements in these perioperative variables could improve medium and long-term postoperative clinical outcomes.

1. Introduction

With the development of new post-processing technologies, there has been an increase in the use of image-guided surgery (IGS) systems to assist surgeons during challenging operations [1,2]. Several preoperative and intraoperative applications of IGS systems are currently available. The most used IGS systems are those that provide preoperative information support, such as segmentation of risk structures or targets by three-dimensional (3D) virtual guidance. IGS systems can also offer intraoperative information support, such as distance visualization, proximity warnings when close to important structures, and augmentation of risk structures or targets [1,2].

IGS systems could improve intraoperative orientation, identification, and location of anatomical structures and their variations, decreasing

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surgeons' workload and contributing to performance enhancement [1, 3–7]. On the other hand, adverse side effects could also arise from the use of IGS systems, such as increased perceived time, pressure and mental demands, errors due to overreliance on the computer assistance, and possible interference on the development of surgical skills [2].

Clinical outcomes, such as patient safety, operation time (OT), intraoperative estimated blood loss (EBL), postoperative hospital stay (POHS), and prevalence of postoperative events (POE) have been reported to improve with the use of IGS systems [1,8–11]. Previous systematic reviews and meta-analyses have reported positive effects of IGS on clinical outcomes of maxillofacial surgery, neurosurgery, and spinal surgery [3–5]. Until now, there are only a few state-of-the-art reviews about the use of 3D-guidance for operations of the lung [12–14], liver [15–17], and kidney [18–21], but no systematic reviews or meta-analyses on the effect of IGS on these solid organs were performed. This meta-analysis aimed to assess the effects of 3D-imaging virtual planning (3DVP) for surgical resection of lung, liver, and kidney nodules.

2. Methods

2.1. Search strategy

This study was reported following Enhancing the Quality and Transparency of Health Research Reporting Guidelines, including the Preferred Reporting Items for Systematic Reviews and Meta-analysis Of Observational Studies in Epidemiology guidelines. We searched all available literature published in the PubMed-MEDLINE, EMBASE, and Cochrane databases through September 31, 2020. The databases were comprehensibly searched using the equivalent terms included in Appendix E1.

2.2. Inclusion and exclusion criteria

Studies were eligible for inclusion if the following criteria were present [1]: comparison of surgical outcomes of lung, liver, or kidney nodule resection surgery with and without image guidance [2]; report of the 3DVP effects on at least one of the following clinical outcomes: operation time, intraoperative bleeding, postoperative hospital stay, or postoperative events [3]; use of preoperative or intraoperative 3D reconstruction from computed tomography (CT) or magnetic resonance images; and [4] design of the study as randomized and non-randomized controlled trials.

Exclusion criteria were the following [1]: studies that used image guidance for biopsy, radiotherapy, or robotic-assisted surgery [2]; studies that used other types of IGS, not the 3D reconstruction, such as augmented reality [3]; case reports, letters to editor, reviews, or meta-analysis [4]; studies not published in English [5]; studies with animals, corpses, or phantoms.

2.3. Study quality assessment

Two reviewers assessed the quality of all eligible studies with the methodological index for non-randomized studies (MINORS) [22]. This tool is composed of 12 items that assess the methodological quality of non-randomized surgical studies. Each of these items is scored from 0 to 2, where 0 indicates that the issue was not reported in the evaluated study, 1 corresponding to items reported inadequately, and 2 correspond to items reported adequately [22].

2.4. Data extraction

Three reviewers independently reviewed all included articles to collect all the primary data (e.g., study design, country of recruitment, type of surgery, nodule site). From each article, the mean operation time (OT), mean estimated blood loss (EBL), mean postoperative hospital stay (POHS), and the number of postoperative events (POE) were extracted. Any disagreements were resolved by consensus.

2.5. Statistical analysis

The effect size (ES) (standardized mean difference, SMD) of 3DVP versus non-3DVP was extracted from each study to calculate the pooled measurements for continuous variables (OT, EBL, POHS). The magnitude of effect for SMD was considered as "small" if equal to 0.2, "medium" if 0.5, and large if 0.8 [23]. The odds ratio (OR) were extracted from each study to combine the pooled results regarding the number of POE. In studies were the standard deviation was not reported, it was estimated based on sample size, median and interquartile range [24]. Data were pooled using a random-effects model.

Heterogeneity between studies was tested with the Q test [25]. The I^2 index was used to quantify the extent of heterogeneity. Publication bias was estimated using the funnel plot and the Egger's and Begg's tests [26, 27]. Sensitivity analyses that excluded each of the individual articles were conducted to evaluate whether any specific study significantly influenced the overall pooled results. All P-values less than 0.05 were considered statistically significant. All statistical analyses were performed using Stata version 15.0 (StataCorp LP, College Station, Texas, USA).

3. Results

3.1. Study characteristics

The initial search yielded 2397 studies, from which 86 were reviewed, and 10 met the inclusion criteria [8–11,28–33] (Fig. 1). The median MINORS score was 17 (interquartile range (IQR), 15.25–17.25). Only one study had a MINORS score lower than 15 (MINORS score = 5) [28].

A total of 897 patients were included, of which 469 (52.3%) subjects had undergone 3DVP, and 428 (47.7%) were non-3DPV controls (eTable 1). Lung was the main surgical site in two studies that performed video-assisted thoracoscopic (VATS) segmentectomy, lobectomy, and bilobectomy [8,28]. Three studies approached liver nodule resection using 3DVP, performing hemihepatectomy, extended hepatectomy, segmentectomy, sectionectomy, or partial resection [9,29,30]. Five studies used image-guided kidney surgery using laparoscopic partial nephrectomy (LPN), robot-assisted partial nephrectomy, or minimum incision endoscopic nephrectomy [10,11,31–33].

3.2. Operation time

All studies were included in the pooled OT analysis [8–11,28–33] (Fig. 2). Six studies described a significant shorter OT for IGS [8–11,29, 30]. In the remaining, there was no significant difference in the OT between IGS and non-IGS [28,31–33]. Pooled analysis revealed a significant difference on OT between the groups with a moderate ES favoring the IGS group and a significantly high heterogeneity between studies (SMD, −0.56; 95%CI: −0.91, −0.22; $I^2 = 83.1\%$; $p < .001$). Visual analysis of the forest plot (Fig. 2) revealed that the article by Xue et al. was the greater contributor to the high heterogeneity between studies. Therefore, we performed a sensitivity analysis with removal of such study, which resulted in a lower but still significant heterogeneity ($I^2 = 52.8\%$; $p = .031$), and a slightly lower effect size (SMD, −0.36; 95%CI: −0.58, −0.15) (Fig. 3).

Nakayama et al. also performed a subgroup analysis of the OT and found that IGS impact was more significant for patients with repeated hepatectomy, as the 3D group presented a 130 min shorter median OT compared to the group without 3D ($p = .03$) [9]. Among the types of hepatic resections, segmentectomy was the only that presented a statistically significant shorter OT for the 3D group (MD, −43.5 min) ($p = .03$) [9].

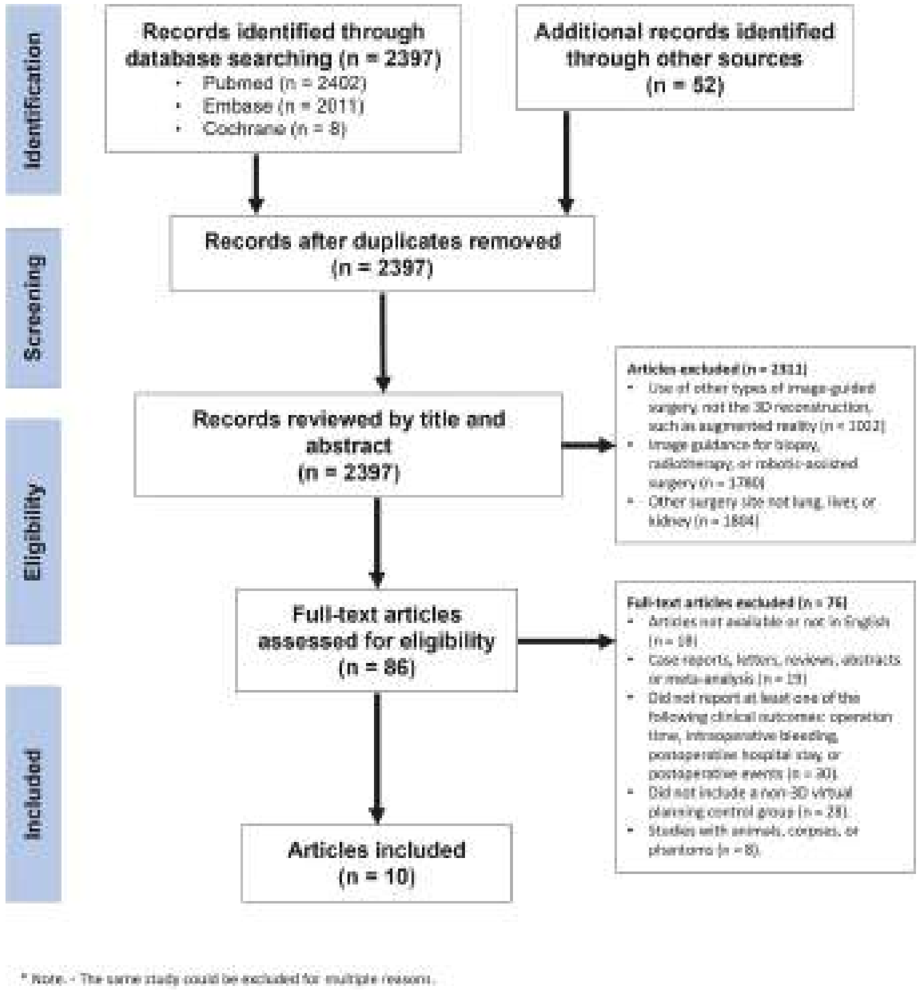

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

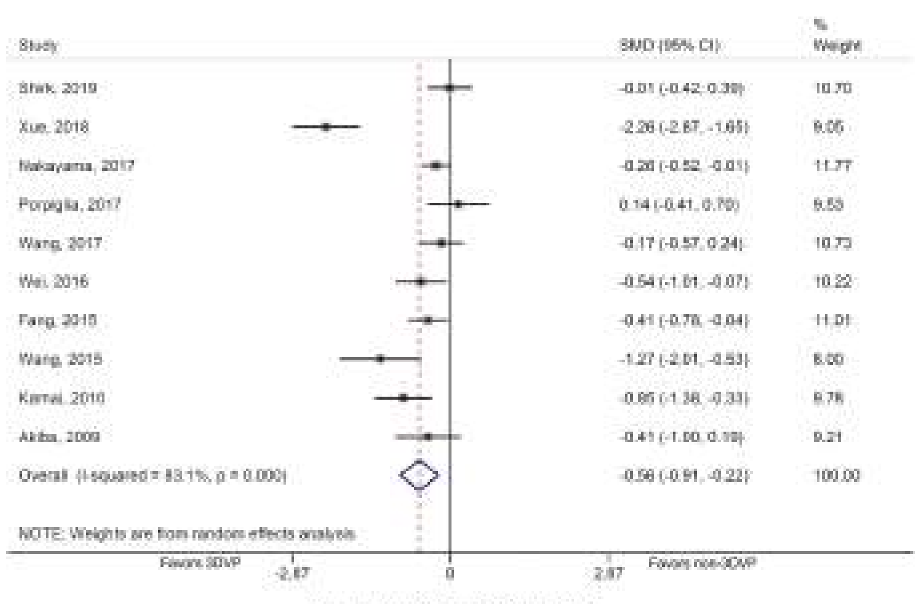

Fig. 2. Forest plot of standard mean difference for operation time.

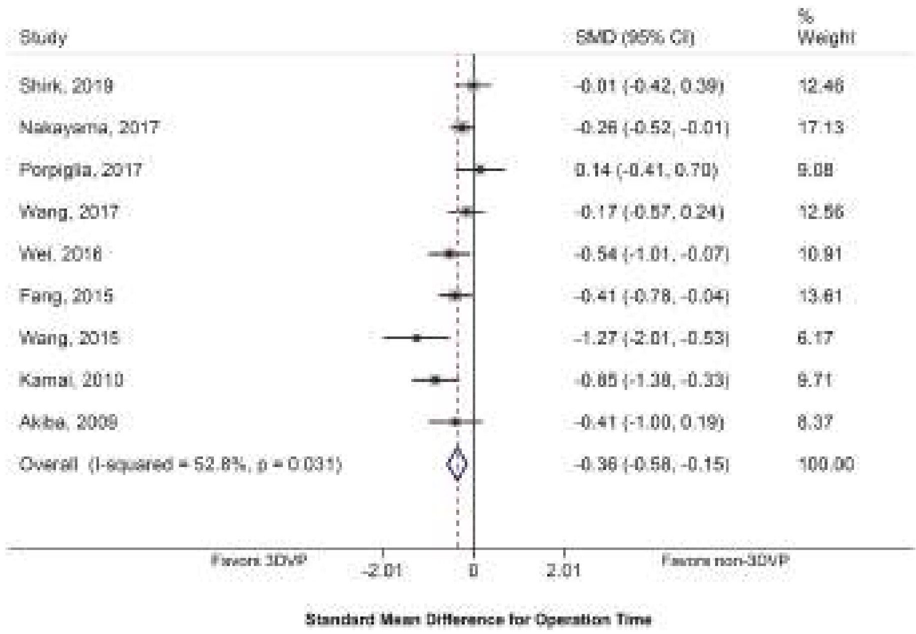

Fig. 3. Sensitivity analysis of standard mean difference for operation time.

Although Wang et al. did not find a significant difference in the mean OT between 3D-guided and non-3D-guided LPN, the authors found a significant shorter OT (MD = −28.1 min; p = .018) for patients with medium-high complexity renal lesions that had a 3D virtual-surgery planning (i.e., R.E.N.A.L. score ≥8) [31]. Likewise, when controlling for case complexity and other covariates, Shirk et al. also found that patients whose surgical planning involved 3-D VR models showed differences in OT (OR, 1.00; 95%CI, 0.37–2.70; estimated OR, 2.47).

3.3. Estimated blood loss

All studies were included in the pooled EBL analysis [8–11,28–33]. Only two studies found a significantly lower EBL for 3DVP [10,11]. There was a significant difference between 3DVP and non-3DVP with a small ES favoring IGS and a non-significant heterogeneity between studies (SMD, −0.18; 95%CI: −0.33, −0.02; I^2 = 22.5%; p = .236) (Fig. 4).

Wang et al. reported a mean EBL of 148.1 (range, 85–290) mL for 3D-guided LPN vs. a mean EBL of 176.1 (range, 80–225) mL for non-3D-guided LPN ($p < .001$) [11]. However, in our pooled analysis, the SMD between the groups in this study was not significant (SMD, −0.56; 95%CI: −1.25, 0.13).

Although Shirk et al. did not find significant differences in EBL between the control and intervention groups, patients without 3D VR-assisted surgical planning were more likely to have EBL greater than 200 mL (OR, 1.98; 95%CI, 1.04–3.78) [33]. In addition, when controlling for case complexity and other covariates, the non-IGS group was more likely to have higher EBL (OR, 1.98; 95%CI, 1.04–3.78; estimated

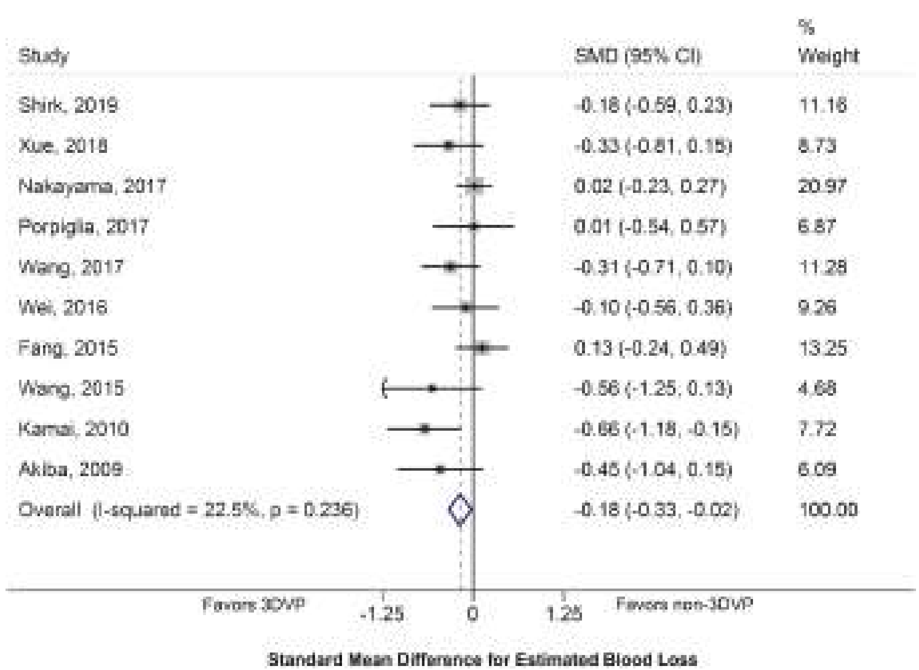

Fig. 4. Forest plot of standard mean difference for estimated blood loss.

OR, 4.56) [33].

3.4. Postoperative hospital stay and postoperative events

Five studies reported the POHS [8,9,11,28,30], and six studies reported POE [8,9,29–32]. None of the studies reported a statistically significant difference in the length of POHS or the number of POE between 3DVP and non-3DVP. The pooled analyses failed to demonstrate any difference between the 3DVP and non-3DVP groups for both POHS (SMD, −0.15; 95%CI: −0.39, 0.10; I^2 = 37.0%; p = .174) (Fig. 5) and POE (OR, 0.80; 95%CI: 0.54, 1.19; I^2 = 0.0%; p = .0973) (Fig. 5).

For lung surgery, PO complications occurred at similar rates for 3D-guided (n = 6; 17%) and non-3D-guided VATS-segmentectomy (n = 5; 16%) in the study by Xue et al. [8]. These included atrial fibrillation, air leakage, pneumonia, and atelectasis. Xue et al. also reported a similar chest tube duration (3D-VATS-segmentectomy, 4.1 ± 1.8 days; vs. non-3D-VATS-segmentectomy, 4.1 ± 2.2 days; p = .93) [8].

Nakayama et al. only defined POE as complications of grade IIIa or higher by the Clavien-Dindo classification [9,34]. Although Fang et al. did not find any significant difference for POE between the groups, non-3D-guided liver resections had significantly more Clavien-Dindo complications of grades III and IV (n = 8; 14.3%; vs. n = 2; 3.3%; p = .048) [30]. Patients that underwent 3D-guided liver resection also had less PO ascites (n = 2; 3.3%; vs. n = 8; 14.3%; p = .048), lower serum total bilirubin (23.2 ± 16.1 g/L; vs. 31.1 ± 24.1 g/L; p = .032), and higher serum albumin (29.3 ± 5.2 g/L; vs 27.8 ± 7.9 g/L; p = .0330) [30].

Two studies on renal nodule resection reported a lower rate of opening of the collecting system and urinary leakage in the 3D-guided nephrectomy groups [31,32]. Wang et al. reported significantly more cases of urinary leakage for patients with medium-high complexity renal lesions (i.e., R.E.N.A.L. score ≥8) that underwent non-3D-guided nephrectomy (4 vs. 0; p = .033) [31]. None of the studies reported significant differences between the IGS and non-IGS groups on renal function, such as a significant increase in serum creatinine level or decrease in ipsilateral glomerular filtration rate postoperatively [31,32]. Although Shirk et al. did not report median POHS for the control and intervention groups, the authors found that patients without 3D VR-assisted surgical planning were more likely to have a length of hospital stay longer than two days (OR, 2.86; 95%CI, 1.59–5.14) [33].

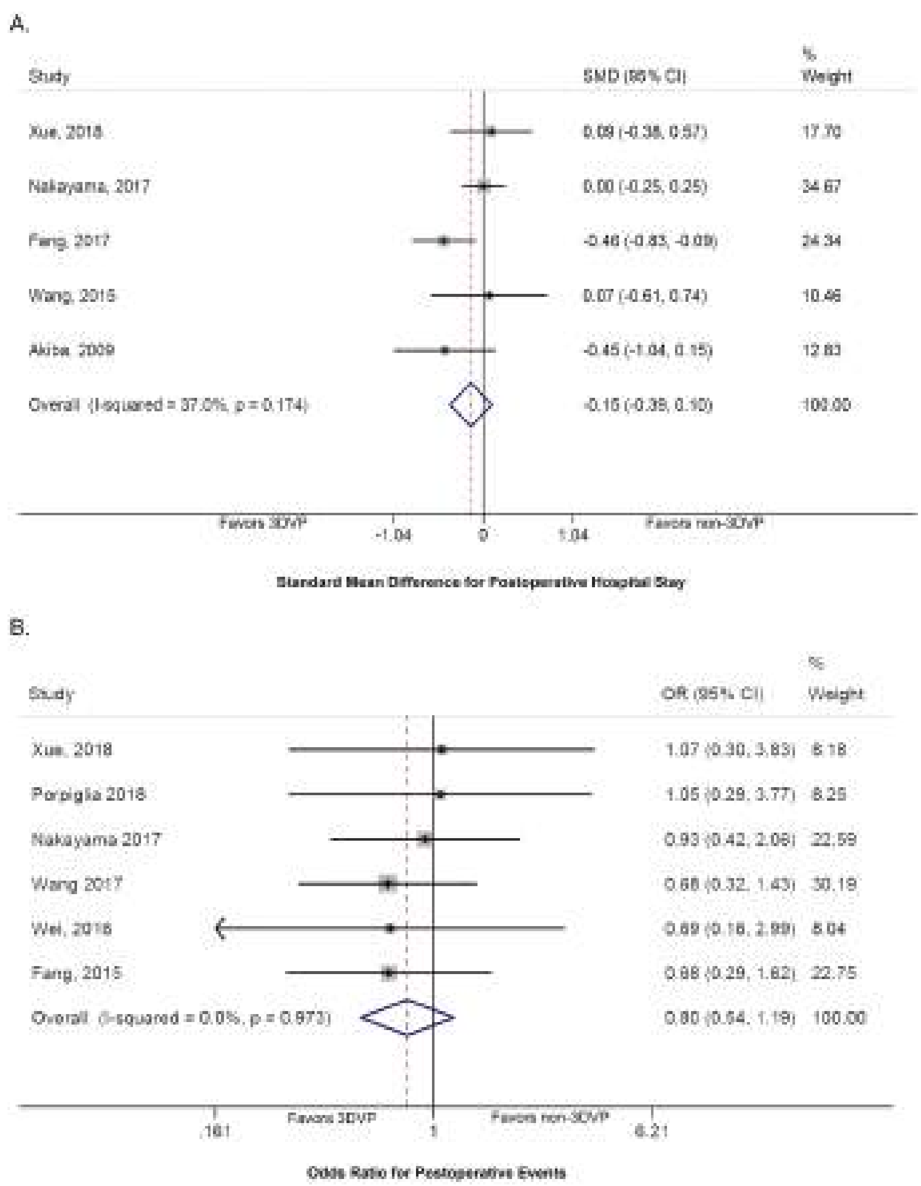

Fig. 5. Forest plots of (A) standard mean difference for postoperative hospital stay and (B) odds ratio for postoperative events.

Further, when controlling for case complexity and other covariates, patients whose surgical planning involved 3-D VR models showed differences in clamp time (OR, 1.60; 95%CI, 0.79–3.23; estimated OR, 11.22), and length of hospital stay (OR, 2.86; 95%CI, 1.59–5.14; estimated OR, 5.43) [33].

4. Discussion

In this meta-analysis, we found that IGS resulted in significantly lower OT and EBL but had no significant impact on POHS and POE. These results demonstrate that 3D-imaging virtual planning could improve some perioperative surgical variables. Although this meta-analysis could not find significant differences in the immediate postoperative clinical outcomes (POHS and POE), improvements in perioperative variables such as OT and EBL could influence medium and long-term clinical outcomes [35–42].

Previous data have shown that prolonged OT was associated with increased risk of the surgical site. In a previous meta-analysis, every additional 10 min, 15 min, 30 min, and 60 min of surgery increased the likelihood of surgical site infection in 5%, 13%, 17%, and 37%, respectively [35]. In another study including over 76,000 patients who underwent laparoscopic procedures, increasing operation time was independently linked with increased odds of complication in several elective procedures, such as colectomy, cholecystectomy, and gastric bypass ([42]).

Also, previous studies have reported worse outcomes associated with higher blood losses during surgery, especially in the kidney [43], liver [44–47], and lung [48–50]. In one series evaluating partial nephrectomy, operative blood loss higher than 250 mL and 1000 mL were associated with 60% and 1150% increased risk of hemorrhagic complications, respectively ([43]). For laparoscopic liver resection, EBL >250 mL has been described to correlate with higher conversion rates to open surgery and overall complications, including liver and kidney failure and postoperative mortality ([44]). In another series including resection of hepatocellular carcinoma, higher blood losses were associated with tumor recurrence and survival ([47]). In our study, we found a small but significant effect size on the use of 3DVP towards minimizing bleeding during surgery. Although this effect was small, techniques that minimize blood losses may benefit nodule resection surgery, reducing complications and postoperative mortality. As 3DVP allows a throughout preoperative evaluation of blood supply and anatomy variations, large blood losses could be prevented, enhancing patient safety.

The use of IGS systems was linked to a reduction of 52% in the number of significant complications and 34% of total complications in a previous meta-analysis on image-guided endoscopic sinus surgery [3]. In another meta-analysis of pedicle screw insertion in spine surgery, the use of IGS systems was associated with a reduction of 61% in the risk of pedicle perforation [51]. However, data for other types of surgery are scarce. To our knowledge, this is the first meta-analysis evaluating only solid organs.

Some concerns have been raised related with the use of IGS systems, as workload increase and impairment on the learning of new surgical skills. For image-guided endoscopic sinus surgery, the previous meta-analysis could not find any significant difference between image-guided and standard surgeries, even when the included studies objectively assessed cardiovascular and endocrine indicators of workload and stress [3]. Also, 3D reconstructions have been shown to impact positively on the surgical education in some papers [52,53]. In our meta-analysis, we did not assess the 3DVP impact on surgeons, but future studies should try to include such analysis.

Our study has some limitations. First, our pooled analysis demonstrated significantly high heterogeneity for the OT ($I^2 = 83.1\%$; $p = .000$) that was reduced in a complementary analysis without the study by Xue et al. ($I^2 = 52.8\%$; $p = .031$) without the loss of the favoring effect towards IGS. Such findings could be attributed to several factors, including the comparison of different organ surgeries, types of surgery, sample sizes, surgeons' experience, software used for reconstruction, and different levels of surgery complexity. However, secondary subgroup analysis to try to identify the sources of heterogeneity, including those mentioned above, could not be performed due to the limited number of studies included in the meta-analysis. However, by using standardized mean differences, we tried to minimize the influence of some of these variables in our analysis. Second, we only included three solid organs that are among the most common sites of resection surgery of nodular lesions. Future studies using other organs could help to validate the benefits of IGS systems further. Third, there were limitations inherent to any meta-analyses, such as selection bias, publication bias, missing information from studies. Finally, most of the included studies were not prospective randomized clinical trials comparing IGS vs. non-IGS.

In summary, our data demonstrated that 3D-imaging virtual planning for resection of lung, kidney, and liver nodules could reduce operation time and estimated blood loss with no effects on immediate postoperative hospital stay and postoperative events.

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Availability of data and material

Data will be provided online once the article after the article is accepted.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

Informed consent

This article does not contain patient data.

Contributions

Matheus Zanon: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Supervision; Validation; Visualization; Roles/Writing - original draft; Writing - review & editing.

Stephan Altmayer: Formal analysis; Investigation; Methodology; Validation; Visualization; Roles/Writing - original draft.

Guilherme Watte: Formal analysis; Investigation; Methodology; Validation; Visualization; Software; Roles/Writing - original draft.

Gabriel Sartori Pacini: Formal analysis; Investigation; Methodology; Validation; Visualization; Roles/Writing - original draft.

Tan-Lucien Mohammed: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Supervision; Writing - review & editing.

Edson Marchiori: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Supervision; Writing - review & editing.

Darcy Ribeiro Pinto Filho: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Supervision; Writing - review & editing.

Bruno Hochhegger: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Supervision; Validation; Visualization; Writing - review & editing.

Declaration of competing interest

The authors declare that they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.suronc.2021.101598.

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