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Current Status of Laparoscopic Surgery in Colorectal Cancer

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Abstract
Purpose of Review We present a review of current status of laparoscopic surgery in the treatment of colorectal cancer. We discuss recent controversies and describe the results of latest minimally invasive techniques and technological innovations.
Recent Findings Despite recent studies questioning the quality of laparoscopic total mesorectal excision, the long-term data currently available continue to support the use of laparoscopy for the treatment of rectal cancer. Laparoscopy can also achieve a complete oncologic resection of T4 colon cancer similar to open surgery in selected patients. However, the evidence for laparoscopic complete mesocolic excision is still limited. Regarding latest techniques, single-incision laparoscopic surgery is not superior to multiport laparoscopy. Robotic surgery provides several technical advantages and short-term benefits. However, cost-effectiveness has not been demonstrated. Transanal total mesorectal excision is a promising technique for distal mesorectal dissection with acceptable short-term patient outcomes.
Summary The oncological safety of laparoscopic excision of colorectal cancer has been widely demonstrated. The critical review of the results obtained with latest techniques will determine which of them will remain as part of the surgical approach in the treatment of colorectal cancer.

This article is part of the Topical Collection on *Surgery and Surgical Innovations in Colorectal Cancer*

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Introduction

The introduction of laparoscopy to cholecystectomy is considered the paradigm of surgical innovation with a successful application of this approach to other procedures [1]. The first laparoscopically assisted colectomy was performed in 1991 [2]. Since then, a large number of randomized trials and meta-analyses have shown that laparoscopic colorectal surgery is associated with less pain, earlier recovery of bowel transit and shorter hospital stay as compared to open surgery [3, 4•, 5–7].

However, implementation of laparoscopic colorectal surgery has been much slower compared to what happened with other procedures such as laparoscopic cholecystectomies. Laparoscopic colorectal surgery is a more challenging operation associated with longer operative times and a long learning curve [7]. Although the adoption of laparoscopy in colorectal surgery has been increasing progressively, the percentage of patients who undergo minimally invasive techniques is still limited revealing that this surgical approach is underused [8].

Another possible obstacle in the progress of laparocopic colorectal surgery was the controversy surrounding the questionable negative impact of tumor recurrence bestowed by this approach during the first years of adoption [9–12]. These initial concerns have been put to rest by results of prospective randomized multicentre studies that showed no differences in the long-term oncological results of laparoscopic surgery compared to the open approach [4•, 13–17]. Moreover, a single-center randomized trial demonstrated a lower recurrence rate and better survival in stage III colon cancer patients undergoing laparoscopic resection compared with open surgery [18]. The use of laparoscopy for the surgical treatment of colorectal cancer is currently widely accepted.

Recent Controversies

Laparoscopic Surgery for Rectal Cancer

Although the benefits in postoperative recovery and adequate oncological outcomes of laparoscopic surgery in the treatment of colon cancer were well supported by randomized controlled trials published several years ago [6, 14, 19], the use of laparoscopy for surgical excision of rectal cancer has been controversial until recently [20]. The technical difficulty of total mesorectal excision (TME) increases in a deep and narrow pelvis and may adversely affect surgical outcomes [7].

Notably, the randomized controlled CLASSIC study included not only patients with colon cancer but also patients undergoing TME for rectal cancer [4•]. The rate of involved circumferential resection margin was higher in the laparoscopic than in the open surgery group (12 vs. 6%), although the difference did not reach statistical significance. On the other hand, patients requiring conversion to open surgery had the highest rates of morbidity and mortality than open or laparoscopy patients. The worse outcomes in this group of patients raised some concerns about the indication of laparoscopy in patients with rectal cancer. The authors concluded that routine use of laparoscopy was not justified in patients with rectal cancer [4•].

Subsequently, other randomized trials and meta-analyses have compared short and long-term clinical outcomes between laparoscopic and open surgery in rectal cancer confirming the short-term benefits and demonstrating the oncological safety of minimally invasive approach in these patients [7] (Table 1). Among these studies, a pivotal one is the European multi-institutional COLOR II trial, in which 1103 patients with rectal cancer were randomized. The authors found no differences in local recurrence and other long-term oncological outcomes between laparoscopic and open surgery [25•].

When it seemed that the controversy was settled, two recent multi-center randomized controlled trials comparing the use of laparoscopic and open surgery to achieve a complete resection of rectal cancer questioned the use of laparoscopy. The ACOSOG Z6051 trial enrolled 486 patients with rectal cancer from 46 surgeons at 35 institutions [26••]. The primary outcome was a composite endpoint of the operation involving three pathological variables: completeness of TME, negative circumferential margin, and negative distal margin. The composite operative success was 81.7% for the laparoscopic group and 86.9% in the open group ($p = 0.41$). The AlaCarRT trial enrolled 475 rectal cancer patients from 24 sites across Australia and New Zealand [27••]. The authors used the same composite endpoint as the ACOSOG Z6051 trial, and all three pathological parameters needed to be satisfied in order to consider the resection was complete. Similar to the ACOSOG Z6051, the primary outcome of a complete resection was achieved in 82% of patients undergoing laparoscopic excision compared to 89% in the open group ($p = 0.38$). Although the rate of complete resection was high in both groups, these two studies concluded that laparoscopy failed to meet the criterion of non-inferiority for pathologic outcomes. According to the authors of both studies, these findings did not support the use of laparoscopy in rectal cancer patients.

These results contradict previous randomized controlled trials and meta-analyses providing level I evidence on the efficacy and equivalent oncologic outcome between laparoscopic and open surgery in patients with rectal cancer. Ludwig and Fichera [28] suggest that based on the CLASSIC trial, the results of the ACOSOG Z6051 and ALaCarRT trials should be interpreted with caution. The CLASSIC trial also initially used surrogate short-term histopathologic endpoints to predict long-term outcomes, and the proportion of patients with positive circumferential resection margin was greater in the laparoscopic group. However, the difference was not statistically significant and, more importantly, no difference in disease-free survival and overall survival was observed between both groups in long-term follow-up [29]. For this reason, it remains to be determined whether the difference in the pathological outcomes in these two recent trials has a significant impact on recurrence. In the meantime, the long-term data that are currently available continue to support the use of laparoscopy as non-inferior to open surgery for the treatment of rectal cancer [28].

Laparoscopic Complete Mesocolon Excision

In the last decade, a new controversy has emerged related to laparoscopic treatment of colon cancer; it is complete mesocolic excision. The aim of this new concept is to harvest the maximum number of lymph nodes draining the tumor. To consider a complete mesocolic excision, it is necessary to perform a central vascular ligation, to remove all the mesentery with its mesenteric fascia and visceral peritoneum, and to resect an adequate length of bowel. Some authors have suggested that this increased in lymph node yield is associated with better oncological outcomes in patients with colorectal cancer [30, 31]. Nevertheless, the feasibility of performing this extensive dissection by laparoscopy has been questioned. To address this issue, a series of 34 prospective, retrospective, and observational studies have been included in a recent systematic review [32•]. The authors concluded that the oncological outcome of laparoscopic complete mesocolic excision is comparable to performing the procedure by an open approach; although, tumors in the transverse colon might be the exception. Other authors, however, have shown that laparoscopic resection for transverse colon cancer is feasible, safe, and comparable to open surgery in terms of short and long term

Table 1 Relevant studies comparing outcomes of laparoscopy and open surgery in patients with rectal cancer

Ref.	N (open vs lap)	Study	Results
Luján, 2009 [21]	204 (103/101)	RCT unicentre	Short term Similar results
Trastulli, 2012 [22]	1544 (703/841)	Meta-analysis	Short term Similar results
Chen, 2014 [23]	953	Meta-analysis	Short term Similar results
Ng, 2014 [24]	278 (142/136)	3 RCT 3 years follow-up	Long term Similar results
Bonjer, 2015 [25•]	1044 (345/699)	RCT multicentre 3 years follow-up	Long term Similar results
ACOSOG Z6051, 2015 [26••]	460 (222/240)	RCT multicentre	Short term Similar results
ALACART, 2015 [27••]	475 (237/238)	RCT multicentre	Short term Similar results

RCT randomized controlled trial

outcomes [33, 34]. Currently, there is not enough evidence to recommend laparoscopic complete mesocolic excision as a routine procedure [35, 36]. Moreover, such an extensive dissection is associated with greater morbidity [37] and long-term survival benefit has not been demonstrated [32•].

Laparoscopic Surgery for T4 Advanced Colorectal Cancer

A locally advanced tumor will be diagnosed in 10–20% of patients with colon cancer [38]. The use of laparoscopic approach for locally advanced T4 colon cancer is a matter of controversy due to the greater technical difficulty, longer operative time and a higher conversion rate which could leads to an inadequate oncologic clearance and worse surgical outcome [14, 39, 40]. The limited evidence in the literature about the correct management of these high-risk tumors makes it difficult to standardize the laparoscopic approach. The final decision to the operative approach rests on the experience of surgical team [41]. A complete preoperative study to design an en bloc resection with contiguously involved structures, including peritumoral adhesions, is required regardless of the approach chosen [42–44].

Several non-randomized studies have compared the short-term and long-term clinical and oncological outcomes obtained by open or laparoscopic approach in patients with T4 tumors [45–49, 50••] (Table 2). In a recent retrospective study, d'Angelis et al. used a propensity score matching analysis and selected 106 patients with T4 colon cancer for each group [49]. Laparoscopic surgery patients showed a faster recovery and shorter hospital stay compared to open surgery patients (10.5 vs. 15.3 days, $p < 0.0001$). Conversion was required in 13 (12.2%) patients and R0 resection was achieved in the majority (>90%) of patients in both groups. There were no significant differences in 5-year disease-free ($p = 0.261$) and overall survival ($p = 0.864$). Elnahas et al. have also performed a retrospective cohort analysis aimed to compare the positive resection margin between both surgical approaches [50••]. Using data from the American College of Surgeons National Quality Improvement Program, the authors selected 455 and 406 patients with T4 colon cancer in the laparoscopic and open group, respectively, and no differences were found with respect to positive margin status (OR 1.10, $p = 0.54$).

The results of these and other studies have shown that laparoscopy can achieve a complete oncologic resection of T4 colon cancers similar to open surgery with an acceptable conversion rate, and conferring the advantages of a faster recovery. Although current guidelines still consider locally advanced disease a contraindication for minimally invasive surgery, or do not even mention this clinical scenario [51, 52], the previously mentioned studies support that laparoscopic resection is a feasible and effective treatment option for selected patients with T4 colon cancer.

Latest Technological Innovations

New minimally invasive surgical techniques and technological innovations have been developed over the last decades. The critical review of the results obtained with these new techniques will determine which of them will remain as part of the surgical approach in the treatment of colorectal cancer.

Table 2 Relevant retrospective studies comparing open and laparoscopic resection for T4 colon cancer

Ref.	N (open/lap)	Study	Results
Huh and Kim, 2012 [45]	43 (24/19)	Matched case-control	Similar short- and long- term outcomes
Kim, 2012 [46]	54 (38/16)	Case control	Similar long-term outcomes
Vignali, 2013 [47]	140 (70/70)	Matched case-control	Similar short- and long-term outcomes
Shukla, 2015 [48]	83 (22/61)	Case control	Similar short- and long-term outcomes
De'Angelis, 2016 [49]	212 (106/106)	Propensity score matching	Similar short- and long-term results
Elnahas, 2015 [50••]	861 (406/455)	Case control	Similar positive margin rate

Single Incision Laparoscopic Surgery (SILS)

As a step forward in laparoscopic surgery, single-incision laparoscopic surgery (SILS) has emerged. In this approach, a single port is used. The main objectives of this approach are to minimize the morbidity associated with the trocars and abdominal wounds, to improve cosmetic results, and also to reduce the inflammatory response to surgical trauma [7].

The use of SILS was first reported during the 90s for the removal of the appendix and gallbladder [53, 54]. However, the first colonic resections with SILS were not published until 10 years later [55, 56]. Although there have been a large number of publications about SILS during the last years, reporting colorectal resections performed in patients with benign diseases and colorectal cancer, the procedure remains controversial. The main limitation of SILS is the need to acquire new skills and also new specifically designed surgical instruments [57, 58]. SILS involves working with straight instruments in parallel and the freedom of movements is limited.

The first retrospective series included a limited number of patients and were aimed to demonstrate the safety of SILS [57, 59, 60]. Thereafter, comparative non-randomized studies were published [61–63]. Although with methodological limitations, all these studies showed that the rates of conversion, morbidity, readmission and mortality of SILS were similar to conventional laparoscopy. Oncological resection outcomes, including the number of retrieved lymph nodes and surgical margins, were also similar to multiport laparoscopic resection. Regarding possible advantages of SILS such as less postoperative pain or better cosmetic results, these studies did not provide sufficient evidence to recommend SILS as a superior strategy compared with multiport laparoscopy [64].

Two prospective randomized clinical trials were published in 2012 comparing SILS with conventional laparoscopy for colorectal cancer. In the study by Huscher et al., 32 patients with colon cancer were included, and the authors found no differences in terms of operative time, mean number of resected lymph nodes, postoperative time or length of hospital stay [65]. The authors concluded that SILS for cancer is a technically feasible and safe oncologic procedure with short-term results similar to those obtained with a traditional laparoscopic approach. By contrast, in another randomized trial including 25 colon cancer patients per group, Poon et al., showed that SILS was associated with less pain and shorter hospital stay [66]. Since then, several systematic reviews with meta-analyses comparing SILS with multiport laparoscopic colectomy have been published [67–70] and all of them have reached the same conclusion: SILS is feasible and safe in patients with colon cancer, but further larger and multicenter trials are needed.

The most recent meta-analysis included 30 studies, published between 2010 and 2015, with a total of 3502 patients with colon resections using SILS in 1068 (30.5%) and multiport laparoscopy in 2434 (69.5%) [71••]. The majority of patients underwent surgery for colorectal cancer. In addition to two randomized controlled, the analysis included eight prospective and 20 retrospective comparative observational studies. There were no significant differences in postoperative morbidity or mortality and the number of harvested lymph nodes was similar between both groups. Because only three studies reported results regarding tumor recurrence, analysis of long-term oncologic result was not performed.

Length of skin incision, mean intraoperative blood loss, recovery of bowel function, and mean postoperative hospital stay significantly favored the SILS group. However, it has to be noted that the body mass index was significantly lower in the single-incision approach group and the number of low anterior resections were significantly higher in the conventional laparoscopy group. These results denote a selection bias which may have influenced the outcomes, as the most complex patients underwent conventional laparoscopic surgery [71••].

A larger randomized clinical trial, not included in previous meta-analyses, has recently been published [72••]. A total of 200 patients were assigned to multiport laparoscopy or SILS. Surgical outcomes were similar between both groups including duration of operation, blood loss, time to first flatus, postoperative stay, and duration of analgesia. The authors concluded that SILS is not superior to multiport laparoscopy. In the absence of data regarding long-term oncological results, it is likely that this study has ended the controversy.

Robotic Laparoscopic Colorectal Surgery

Despite the revolution that involves laparoscopic surgery in colorectal cancer, this approach still has limitations related to the loss of tactile sensesory input, two-dimensional view with unstable video, worse dexterity, and a limited range of motion of surgical instruments, which is especially important in challenging advanced procedures in small anatomical spaces. In an attempt to overcome some of these limitations, the robotic surgery was introduced in our armamentarium in 1985. The Da Vinci™ robotic surgical system (Intuitive Surgical, Inc, Sunnyvale, Calif) obtained FDA approval in 2000, and the continuous advances and modifications of its technology have revolutionized this field [73•, 74].

Robotic surgery provides several technical advantages including enhanced dexterity and maneuverability and magnified three-dimensional view, which improves the accuracy and depth of sensation. As a result of the introduction of EndoWrist instruments, seven degrees of freedom are experienced with robotic surgery. Thanks to these characteristics, the DaVinci™ system diminishes the physical stress for surgeons and allows a shorter learning curve with a faster acquisition of skills to perform challenging interventions. In fact, robotic pelvic surgery was promoted as being more quickly mastered after 25 to 35 cases [75]. Its application in colorectal surgery is relatively new. The first robotic colectomy was performed in 2001 by Weber et al., [76] and the first robotic rectal resection in 2006 by Pigazzi [77]. Since then, several original studies and meta-analyses have demonstrated its safety and efficacy, and have suggested some benefits over the laparoscopic approach such as lower intraoperative blood loss and lower conversion rate with a similar morbidity and comparable oncological accuracy of resection [78, 79, 80••, 81, 82•]. A recent meta-analysis published by Zhang et al. [83••] including 3318 patients with colon and rectal cancer established lower conversion rate, lower blood loss and shorter hospital stay with no differences in morbidity and pathological outcomes of robotic vs. laparoscopic surgery. Furthermore, some surgeons advocate the superiority of robotic surgery for some specific steps during the colectomy as the lymphadenectomy or the ability to perform intracorporeal anastomoses [84, 85].

Specifically related to rectal cancer, recent studies have failed to demonstrate inferior morbidity outcomes with the robotic approach. Thus, it has been suggested that robotic rectal surgery could offer better short-term outcomes only in selected cohorts such as male and obese patients with distal rectal tumors [86]. Several international multi-center prospective randomized trials such as ROLARR (Robotic versus LAparoscopic Resection for Rectal Cancer trial [ClinicalTrials.gov ID: NCT01736072]) are currently evaluating the benefits and indications of robotic surgery in the treatment of rectal cancer. The preliminary results presented thus far have shown no statistically significant differences in operative, oncologic or functional outcomes. In contrast, concerning data in terms of incomplete mesorectal resection rates have emerged (21.4% laparoscopic vs 23.2% robotic) [87••]. Other studies have also found concerning results in the quality of TME and other surrogates of adequate oncologic surgery compared with the laparoscopic resection [88, 89•]. Nonetheless, other groups have observed better clearance at the circumferential margin with the robotic approach [73•, 90, 91]. Similarly, the possible benefits of robotic surgery regarding urological and sexual dysfunction have to be analyzed in large prospective studies [78, 92, 93]. As of today, there is lack of conclusive evidence of the clinical benefits and long-term oncological safety of robotic surgery over conventional laparoscopy (Table 3).

With increasing use of robotic surgery, other limitations have been emerged. For instance, the surgeon loses the tactile sensitivity; therefore, new visual skills have to be acquired to perform the procedure safety. Also, the patient has to be in an optimal and stable position that cannot be changed after the docking. This issue is an important one in colorectal surgery, where it is necessary to access different areas of the abdomen during the procedure. However, it has been shown that operative time decrease rapidly with experience.

Finally, the cost of robotic surgery is a major problem for any health system and has contributed greatly to delay its implementation and widespread use in colorectal surgery. The cost could be as high as three times than that of laparoscopic surgery [94]. A comparative cost-effective study published by Ramji et al. [95] concluded that the cost of laparoscopy is lower than open surgery and the cost of robotic surgery is the highest. Several other studies have found that overall hospitalization costs were significantly higher for robotics due to the equipment costs, maintenance, operating costs and the operation related consumables [74, 85, 96]. Although there is a reduction in hospital stay, this fact does not compensate the greater cost. Thus, we can conclude that cost-effectiveness of robotic surgery for colorectal cancer has not been demonstrated [80••, 97]. In spite of the increasing use of the robot, it can only be recommended for selected cases in highly specialized centers with an important volume to justify the cost [98].

Natural Orifice Transluminal Endoscopic Surgery

Natural Orifice Transluminal Endoscopic Surgery (NOTES) emerged in order to improve even more the results of laparoscopic surgery. The principal characteristic of NOTES is the use of natural orifices to access to the peritoneal cavity through flexible endoscopies or laparoscopic rigid instruments [99].

The first successful transanal NOTES sigmoidectomy was published in 2007 in a cadaveric model, using transanal endoscopic microsurgery (TEM) instrumentation [100]. Later on, Velhote et al. [101] published, in 2009, the first sigmoidectomy by a transanal approach. This method has

Table 3 Relevant studies comparing the use of robot and laparoscopy in patients with rectal cancer

Ref.	N (lap vs robot)	Study	Results
Yang, 2012 [82•]	1493 (929/564)	Meta-analysis	Short term
			Lower blood loss and conversion rate
			No difference in morbidity
Liao, 2014 [81]	226 (116/110)	Meta-analysis	Short term
			Lower blood loss and conversion rate.
			Similar postoperative and pathological results
Speicher, 2014 [89•]	6403 (5447/956)	RCT multicenter	Short term
			Similar results
Park, 2015 [88]	217 (84/133)	RCT	Long term
		5 years follow-up	Similar results
Kim, 2015 [80••]	66/33	RCT	Short term
			Similar results
Broholm, 2015 [92]	689 (161/152)	Meta-analysis	Better urogenital function
Zhang, 2016 [83••]	3318 (1466/1852)	Meta-analysis	Short term
			Similar results

RCT randomized controlled trial

undergone a great deal of development in recent years especially as a hybrid technique combined with the use of conventional laparoscopic trocars. The natural orifices commonly used by colorectal surgeons have been the vagina [102] and the anus [103]. A recent German study including the first 139 colonic NOTES procedures, transvaginal or transrectal has shown that NOTES colectomy is feasible and can be performed safely [104].

More recently, several colorectal surgeons have used NOTES through the anus assisted by laparoscopy to perform a TME. The use of NOTES for TME is a combination of the benefits of TEM with the improvements achieved with Transanal Minimally Invasive Surgery (TAMIS). For this reason, this approach has received different names: Transanal NOTES for TME, Transanal endoscopic TME, Perirectal NOTES, TAMIS-TME or more recently Ta-TME.

TEM was first described in 1983 [105] and has become a widely accepted alternative to excise premalignant and early stage rectal cancer through the anus. The development of this approach offers advantages compared to endoscopic submucosal dissection [106] or transanal local excision [107]. Moreover, it is a feasible alternative to radical resection of low risk T1 adenocarcinoma of the rectum [108]. It can also be substantially advantageous in patients who are medically unfit or refuse radical surgery. In 2010, Atallah et al. described a modification of TEM named TAMIS consisting in the use of a single port laparoscopic device transanally instead of the rectoscope of the TEM [109]. Some of the advantages of TAMIS are the quicker settling of the operative field and lower cost compared to TEM [7].

The recent interest in NOTES combined with minimally invasive surgery allows the transanal endoscopic rectal resection including complete mesorectal excision. The feasibility and safety of this procedure has been demonstrated first in animal models [110–112] and also in human cadavers [113, 114]. In 2010, Sylla and Lacy reported the first case of a transanal NOTES rectosigmoid resection assisted by laparoscopy [115]. Since then, several case series of patients treated with TaTME have been published showing that this is a safe and reproducible procedure which does not negatively impact the surgical oncological or functional outcomes [115, 116, 117••, 118].

Lacy and co-workers [117••] published the first prospective cohort study of rectal cancer patients treated by TaTME compared to a retrospective historical cohort treated by laparoscopic TME. The results of this study established the feasibility and safety of TaTME technique. In this study, the authors found no differences in postoperative morbidity, but compared to laparoscopic TME TaTME was associated with a shorter operative time and a lower readmission rate.

An international registry including the first 720 cases from 66 registered units in 23 countries has been recently published [119••]. Abdominal or perineal conversion was 6.3 and 2.8%, respectively. Intact TME specimens were achieved in 85% and R1 resection rate was 2.7%. Postoperative mortality and morbidity were 0.5 and 32.6% respectively. The authors concluded that TaTME was an oncologically safe and effective technique for distal mesorectal dissection with acceptable short-term patient outcomes and good specimen quality.

TaTME compared to other NOTES approaches might have some specific advantages. First, TaTME allows avoiding an extra viscerotomy, because the proctotomy used to remove the specimen could be part of the anastomosis. Second, it also offers a better view of the distal edge of the tumor facilitating a clear distal resection margin. Finally, this approach avoids abdominal incisions with its associated morbidity [120]. TaTME would seem to be especially indicated for specific high risk patients such as: man, obese, as well as patients with a narrow pelvis and bulky tumors [117••, 121]. However, randomized controlled trials are needed to assess the short and long term results of this new technique [122].

Conclusion

Laparoscopic colorectal surgery is associated with short-term benefits as compared to open surgery without differences in the oncological outcomes. The long-term data currently available support the use of laparoscopy for surgery of rectal cancer and selected patients with T4 colon cancer. However, the evidence for laparoscopic complete mesocolic excision is limited. The critical review of latest minimally invasive techniques and technological innovations will determine which of them will remain as part of the surgical approach in the treatment of colorectal cancer.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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