

Appendix 1.

This review of the literature was modeled on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and identical to a previous performed systematic review.^{1,2} Since the literature search from the previous publication on this topic ended on September, 2012, we included dates from October 1, 2012 to October 31, 2019. Each abstract was evaluated and all pertinent references from the manuscripts were obtained. The strength and quality of evidence was defined by using GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) terminology and finalized by consensus among all the authors.³ (Table 1) From 4,482 abstracts retrieved by our search, we identified 216 RCTs, meta-analyses or systematic reviews since October 1, 2012.

All technical aspects of CD with recommendations, corresponding GRADE strength of evidence and references are summarized in order of performance (or omission) in Table 2. References noted in this Table include all RCTs, meta-analyses or systematic in the current systematic review as well as those from the prior systematic review.² The Commentary reviewed all CD surgical steps that can be incorporated by the surgeon and the Appendix includes those that can be incorporated by institutions.

CESAREAN DELIVERY SURGICAL TECHNIQUE: INSTITUTIONAL CONSIDERATIONS

PROPHYLACTIC ANTIBIOTICS

Dahlke JD, Mendez-Figueroa H, Maggio L, Sperling JD, Chauhan SP, Rouse DJ. The case for standardizing cesarean delivery technique: seeing the forest for the trees. *Obstet Gynecol* 2020;136.

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Thirteen additional RCTs or reviews have been performed since the fourteen previously reviewed.^{2,4-30} These trials affirm previous recommendations for standardized pre-incision administration of ampicillin or first generation cephalosporin up to 60 minutes prior to cesarean. Notably, two well-designed and powered RCTs expand antibiotic coverage in specific patient populations. Tita et al. reported a significant reduction in endometritis, wound infection, and serious maternal adverse events when 500mg IV azithromycin was added pre-operatively in those undergoing cesarean delivery during labor or after membrane rupture.¹⁴ In those with a pre-pregnancy BMI ≥ 30 , Valent et al. found a similar reduction in surgical site infection with the addition post-operative use of oral cephalexin 500mg and metronidazole 500mg every 8 hours for a total of 48 hours following delivery.¹⁵

Recommendation: Pre-incision Ampicillin or 1st generation cephalosporin, add Azithromycin 500mg IV x1 if labored

THROMBOPROPHYLAXIS

Similar to those studies included in the previous review, there remains a paucity of data on the benefit of thromboprophylaxis during CD.³¹⁻³³ There were no additional clinical trials of compression stockings and/or pneumatic compressions stockings nor any comparison of these modalities to heparin as in the previous review. One small RCT assessed the effect of intermittent pneumatic compression devices on markers of fibrinolysis, with no difference between groups seen.³⁴ The risk of CD associated venous thromboembolism (VTE) is estimated to be 0.23%, and trials performed to date remain underpowered to provide recommendation

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guidance.³⁵ Both the American College of Obstetricians and Gynecologists (ACOG) and Society for Maternal Fetal Medicine (SMFM) recommend all women who undergo CD receive sequential compression devices intraoperatively based on low-quality evidence as the benefits of this intervention outweigh its risk or burden.^{36,37}

Recommendation: Sequential compression devices prior to surgery

LATERAL TILT

Previously, there was insufficient data to recommend left lateral tilt based on five studies.² Since then, one RCT and one systematic review has been performed.^{38,39} In the RCT, Lee et al. found that left lateral tilt position had no effect on neonatal acid-base status.³⁸ The Cochrane review by Cluver et al. similarly found limited evidence to support or disprove the value of the use of tilt, noting variable quality and sample sizes in the studies analysed.³⁹

Recommendation: Omit Left lateral tilt

WARMING INTERVENTIONS

Warming interventions such as ambient room temperature and intravenous fluid warming was not reviewed in the previous systematic review.² Proposed benefits of these interventions include reduction of neonatal and maternal hypothermia and comfort. Three RCTs and two systematic reviews have been performed to assess these interventions.⁴⁰⁻⁴⁴ In general, operating room temperature of 23°C (73°F) reduces the rate of neonatal and maternal

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hypothermia and appears superior to active warming such as forced air warming or under body carbon-polymer mattresses.

Recommendation: Standardized maternal active warming interventions

SUPPLEMENTAL OXYGEN

Supplemental Oxygen during cesarean was previously not recommended with a high level of certainty.² Three addition RCTs and one meta-analysis confirmed no significant outcome differences, in particular, on the rate of surgical site infection or neonatal umbilical cord gases.⁴⁵⁻⁴⁸

Recommendation: Omit Supplemental Oxygen

PRE-OPERATIVE ENEMA

One RCT addressing pre-operative enema in scheduled cesareans was performed with no benefit in bowel function or reduction in complications when this is performed.⁴⁹

Recommendation: Omit Preoperative enema

SKIN PREPARATION

Previously, skin preparation with either chlorhexidine-alcohol (CHG) or Iodine was recommended, as there was insufficient evidence to favor one method over the other.² Since then, four RCTs and three systematic reviews have been performed.⁵⁰⁻⁵⁶ Regarding the RCTs,

Tuuli et al. and Kunkle et al. demonstrated benefit in reduction of surgical site infection with

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CHG, while Ngai et al and Springel et al. demonstrated no difference in preparation type.⁵⁰⁻⁵³ In two reviews, there was insufficient evidence to recommend one preparation over another, while Tolcher et al. demonstrated benefit of CHG.⁵⁶ Our synthesis of this data suggests that CHG is certainly non-inferior to povidone iodine, with evidence to suggest significant benefit.

Recommendation: Skin preparation with chlorhexidine-alcohol

VAGINAL PREPARATION

Previously, preoperative vaginal preparation with iodine was recommended with moderate level of certainty.² Since then, three RCTs and three systematic reviews have been performed, confirming the benefit of vaginal preparation in reduction of post-cesarean morbidity from infection (primarily endometritis) in those who have labored prior to cesarean.⁵⁷⁻⁶² In the most recent Cochrane review, the vast majority of trials used povidone-iodine rather than chlorhexidine-based solutions with benefit noted in reduction of post-cesarean endometritis, fever, wound infection, or composite wound complications.⁶⁰

Recommendation: Vaginal preparation with Povidone-iodine if labored

INDWELLING BLADDER CATHETER

There was previously insufficient evidence to recommend pre-operative placement of an indwelling bladder catheter, or optimal timing of removal, if placed.² Three additional RCTs and a Cochrane review have been published.⁶³⁻⁶⁵ In a Cochrane review, there was insufficient evidence to support specific timing of placement.⁶⁶ The three RCTs compared various removal

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timings, from immediate to 24 hours. In general, early removal was associated with earlier ambulation, fewer urgency symptoms and possible lower risk of infection with no difference in adverse outcomes such as urinary retention.

Recommendation: Indwelling bladder catheter- pre-operative placement with removal when feasible post-operatively

INCISIONAL ADHESIVE DRAPES

In the previous review, use of incisional adhesive drapes were not recommended with a moderate level of certainty based on two trials. These drapes contain adhesive over the entire surgical field through which the surgeon makes their incision. There has not been any additional RCTs addressing the optimal sterile dressing during CD and this technique was included one Cochrane review and another meta-analysis.^{54,67} The meta-analysis included 1943 subjects and demonstrated an increased risk of wound infection when incisional adhesive drapes were utilized, and therefore not recommended.⁶⁷

Recommendation: Omit incisional adhesive drapes

BARRIER RETRACTORS

In the previous review, one RCT was included that assessed the utilization of a self-retaining retractor for reduction of SSI, in particular women with obesity.² Since then, three RCTs and one systematic review has assessed the use of barrier retractors with minimal benefit in SSI reduction compared to standard hand held retractors.⁷⁶⁻⁷⁹

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Recommendation: Omit self-retaining barrier retractors

UTERINE ATONY PREVENTION

Oxytocin 10-40 IU over 4 to 8 hours was recommended for prevention of uterine atony with moderate level of certainty based on 15 RCTs or systematic reviews/meta-analyses.² Given the significant morbidity associated with hemorrhage, it was noted that evaluating methods for minimizing CD-associated blood loss should be a research priority. In the past seven years, there has been a remarkable 38 RCTS and 10 Systematic reviews/meta-analyses on this technical aspect of CD.⁸⁸⁻¹³⁵

Medications evaluated and/or compared include oxytocin, misoprostol, tranexamic acid (TXA), carbetocin and in one trial, a traditional Chinese medication Yimucao. Some of these contemporary trials compare efficacy between these medications, while other trials compare dose, route or timing of the administration of a single medication. Based on these trials, there is insufficient evidence to change previous recommendations for Oxytocin 10-40 IU over 4-8 hours for uterine atony prevention.

TXA remains one of the most compelling and controversial interventions for prevention of postpartum hemorrhage as evidenced by five additional trials and five systematic reviews. Simonazzi et al. performed a systematic review and meta-analysis of nine trials that included 2,365 women and found those who received TXA has significantly less blood loss, lower hemoglobin drop and low severe postpartum hemorrhage compared to controls.¹²¹ In contrast, in a systematic review by Ker et al., the authors note that the quality of randomized trials to

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date remain questionable, from inadequate sample size to inadequate randomization, to data quality concerns.¹²² To this point, a search of registered clinical trials of tranexamic acid and cesarean (clinicaltrials.gov) resulted in 19 active trials that are recruiting patients in the United States and abroad. We look forward to the findings of these trials and withhold changing our recommendation until further data is available.

Recommendation: IV Oxytocin 10-40 IU over 4-8 hours

SURGICAL NEEDLE TYPE

Blunt tip surgical needles was previously recommended in based on one RCT and a Cochrane review, which also included surgeries other than CD.² Since then, one additional RCT has been performed that did not demonstrate a different in the rate of glove perforation between groups and improved surgeon satisfaction with sharp surgical needles.¹⁷⁶ In contrast, the prior Cochrane review demonstrated a reduction of one glove perforation for every six surgeries. If available, we believe the safety benefit of blunt surgical needles outweigh the surgeon preference of sharp surgical needles.

Recommendation: Blunt surgical needle, if available

WOUND DRESSING

Optimal wound dressing was not addressed in the previous systematic review.² There has been seven RCTs since that address this aspect, primarily timing of dressing removal or comparing standard post-surgical dressing with a commercial wound dressing.²⁰³⁻²⁰⁸ These

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include material with dialkylcarbamoyl chloride (DACC), aloe vera gel, topical scar (extract of *Allium cepae*, allantoin, and heparin), silver nylon, and tissue adhesive. Currently, there is not compelling evidence to recommend any of these over standard wound dressing.

Recommendation: Standard post-surgical wound dressing

NEGATIVE PRESSURE WOUND THERAPY

Prophylactic negative pressure wound therapy in women with obesity (BMI >30) was also not addressed in our previous review. Since then, 5 RCTs and 3 systematic reviews have been performed.²⁰⁹⁻²¹⁶ In one systematic review, CD was one of several surgical procedures that assessed benefit of this modality. Two systematic reviews published during similar times demonstrated conflicting findings, with Yu et al. suggesting a reduction in surgical site infection and wound complications and Smid et al. suggesting no benefit.^{209,210} Two additional RCTs after these systematic reviews further demonstrated no significant difference in this dressing type, even in those women with Class II or III obesity.^{213,214}

Recommendation: Omit negative pressure wound therapy

OTHER CD TECHNIQUES

In addition to those RCTs reviewed, additional technical aspects assessed by includes a family oriented (direct visualized of birth, cutting the umbilical cord, early skin-to-skin contact) approach to cesarean (Charité cesarean), extraperitoneal technique, modified sodium hyaluronic acid-carboxymethylcellulose for the reduction of adhesion formation, reiki or prayer

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for reduction of postoperative pain, grape seed extract for improved wound healing, elective appendectomy, and routine instrumented delivery.^{217-220,272, 331,332} At this time, there is insufficient evidence to recommend these approaches.

Recommendation: Omit Charité technique, modified sodium hyaluronic acid-carboxymethylcellulose, reiki/ prayer for reduction of postoperative pain management, grape seed extract ointment for improved wound healing, elective appendectomy, routine instrumented delivery

CONCLUSION

In this updated review, we have outlined current evidence for each technical aspect of CD surgical technique. The Commentary reviewed all CD surgical steps that can be incorporated by the surgeon and the Appendix includes those that can be incorporated by institutions. In addition to the 155 studies from 1960-2012 previously reviewed², we have included an additional 216 RCTs, systematic review/meta-analyses and Cochrane reviews completed from October 2012 through October 2019. That is to say, there have been more studies on this topic in the past 7 years than the previous 50 years combined. Our recommendations, quality of evidence and references for each CD technique is summarized in the Table 2.

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Table 1. GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) Quality of Evidence Rating Definitions³

Grade	Clarity of Risk/Benefit	Quality of Evidence	Implication
1A: Recommendation: Strong Evidence: High-quality	Benefits clearly outweigh risks and burdens, or vice versa	Consistent evidence from well performed, randomized controlled trials (RCTs), or overwhelming evidence of some other form. Further research is unlikely to change confidence in the estimate of benefit and risk.	Strong recommendation that can apply to most patients in most circumstances without reservation. Clinicians should follow unless a clear and compelling rationale for an alternative approach is present.
1B. Recommendation: Strong Evidence: Moderate-quality	Benefits clearly outweigh risks and burdens, or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on confidence in the estimate of benefit and risk and may change the estimate	Strong recommendation that applies to most patients. Clinicians should follow unless a clear and compelling rationale for an alternative approach is present
1C. Recommendations: Strong Evidence: Low-quality	Benefits appear to outweigh risks and burdens, or vice versa	Evidence from observational studies, unsystematic clinical experience, or RCTs with serious flaws	Any estimate of effect is uncertain. Strong recommendation that applies to most patients. Some evidence supporting recommendation is low quality

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2A. Recommendation: Weak Evidence: High-quality	Benefits closely balanced with risks and burdens	Consistent evidence from well performed RCTs or overwhelming evidence of some other form. Further research is unlikely to change confidence in the estimate of benefit and risk	Weak recommendation; best action may differ depending on circumstances or patients or societal values.
2B. Recommendations: Weak Evidence: Mild-quality	Benefits closely balanced with risks and burdens; some uncertainty in the estimates of benefits, risks, and burdens	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design Further research is likely to have an effect on confidence in the estimate of benefit and risk and may change the estimate	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances.
2C. Recommendation: Weak Evidence: Low-quality	Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens.	Evidence from observational studies, unsystematic clinical experience, or RCTs with serious flaws. Any estimate of effect is uncertain.	Very weak recommendation, other alternatives may be equally reasonable.
Best practice	Recommendation in which either (i) there is an enormous amount of indirect evidence that clearly justifies strong recommendation (direct evidence would be challenging, and inefficient use of time and resources, to bring together and carefully summarize), or (ii) recommendation to the contrary would be unethical.		

Data from Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924-926. doi:10.1136/bmj.39489.470347.AD

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Table 2. Evidence-based Recommendations for Cesarean Technique

Cesarean Delivery Technique	Recommendation	Grade*	References
Prophylactic antibiotics	<ul style="list-style-type: none"> • Pre-incision Ampicillin or 1st generation cephalosporin • Add Azithromycin 500mg IV x1 if labor before CD 	1A	4-30
Thromboprophylaxis	Sequential compression devices prior to surgery	2B	31-37
Lateral tilt	Omit	2A	38,39 295-299
Warming interventions	Standardized maternal active warming interventions	1C	40-44
Supplemental oxygen	Omit	1A	45-48 243, 244
Pre-operative enema	Omit	1C	49
Skin preparation	Chlorhexidine-alcohol	1A	50-56 300, 301
Vaginal preparation	Povidone-iodine if labored	1A	57-62 221-223
Indwelling bladder catheter	Pre-operative placement, removal when feasible post-operatively	1B	63-66 224-229
Incisional Adhesive Drapes	Omit	2B	54,67 302, 303
Skin, subcutaneous, fascia and peritoneum entry	Transverse, 2-3 cm above pubic symphysis, sharp subcutaneous and fascia dissection, omit superior and inferior fascia dissection, blunt subcutaneous and fascia expansion, blunt peritoneal entry	1A	68-75 230-236, 304-314
Barrier retractors	Omit	1C	76-79 245
Bladder flap development	Omit	1A	80-82 237-239 315
Uterine incision and expansion	2-3 cm low transverse sharp incision, blunt entry, cephalad-caudad expansion	1A	83-87 240-242 316-323

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Instrumented Delivery	Omit	2A	324, 325
Uterine atony prevention	Oxytocin 10-40 IU over 4-8 hours	1A	88-135 246-258 326-328
Placenta removal	Spontaneous	1A	136-139 259 329-334
Intrauterine wiping	Perform only when placental membranes seen	2B	140
Routine cervical dilation	Omit	1B	141-145 268-270
Uterine repair: In situ or exteriorized	Exteriorize	1B	146-151 260-267 335-339
Uterine closure	Single layer	1B	149-165 271 350-353
Elective Appendectomy	Omit	1C	273
Intra-abdominal irrigation	Omit	1C	166,167 273, 274, 301
Peritoneal closure	Omit	1A	168-170 275-283 149-151 345-355
Rectus muscle reapproximation	Omit	1C	170
Glove change	Omit	2B	171-175
Surgical needle type	Blunt, if available	1B	176, 284, 285
Fascia closure	Running, with delayed absorbable suture	2B	177,178
Subcutaneous tissue irrigation	Perform	2B	179
Subcutaneous tissue closure	Suture closure if ≥ 2 cm depth	1A	180-182 286, 287 356-363
Skin closure	Subcuticular, absorbable monofilament suture	1A	183-202, 288-295, 340-343, 364, 365
Wound dressing	Standard post-surgical wound dressing	1B	203-208

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Negative pressure wound therapy	Omit	2B	209-216
Other techniques: Charité technique, modified sodium hyaluronic acid-carboxymethylcellulose, reiki/prayer for reduction of postoperative pain management, grape seed extract ointment for improved wound healing, elective appendectomy, routine instrumented delivery	Omit	2C	217-220, 272, 331, 332

***See Table 1.**

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