

ONCOLOGIC OUTCOMES OF LAPAROSCOPIC AND OPEN COLORECTAL CANCER SURGERY

META-ANALYSIS AND CORRELATION WITH EXPERT OPINION

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BACKGROUND

- Laparoscopic surgery is increasingly used to treat colorectal cancer
- Survival and oncologic outcomes are most important in evaluating this technology
- Numerous RCTs have been conducted, but no good review of survival data
- Unclear whether surgeons adoption of this technology has relied upon survival evidence

STUDY CRITERIA

- Systematic review and meta-analysis

Population	Patients with colorectal cancer
Intervention	Laparoscopic surgery
Control	Open surgery (laparotomy)
Primary Outcome	Survival
Secondary Outcomes	Operative, postoperative, long-term, QoL
Study Types	RCTs, observational, reviews, guidelines, chapters

1991-2009

SEARCH STRATEGY

- Electronic search strategy devised with librarian, high sensitivity
- 6 major databases, 13 minor databases
- Snowball technique: manual reference list review and forward citation linkage since 2008
- 9 major textbooks (all editions since 1991)
- No language limitation

DATA MANAGEMENT

- Articles screened and reviewed for inclusion
- Included articles were abstracted into forms
- Non-English papers translated with Google Translate
- RCT data was synthesized and pooled where appropriate using standard methods
- RevMan 5, random effect models

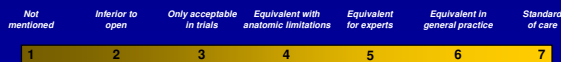
META-ANALYSIS OF SURVIVAL DATA

- Time-to-event (survival) data difficult to pool, as must use hazard ratio (rarely available)
- Continuous or dichotomous outcomes not not reliable, difficult to interpret
- Used published methods to get estimates of $\ln(\text{HR})$ and $\text{var}(\ln(\text{HR}))$ from individual papers
- Pooled $\ln(\text{HR})$ using inverse variance method and random effect model

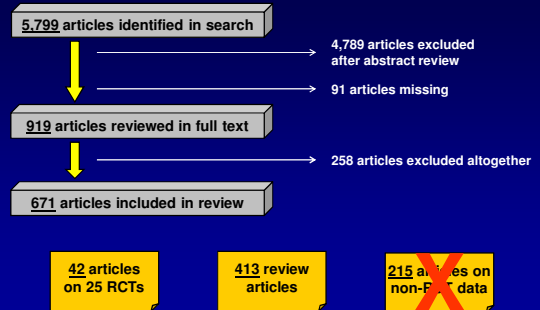
Parmar 1996, *Statist Med*
Williamson 2002, *Statist Med*
Tierney 2007, *Trials*

ANALYSIS OF EXPERT OPINIONS

- Review articles as a measure of expert opinion
- Included article if addressed laparoscopy for colorectal cancer OR if addressed surgical treatment of colorectal cancer
- Used Likert scale to derive the author's opinion regarding value of laparoscopy (in addressing the primary outcome)



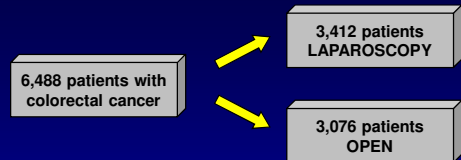
STUDY FLOW CHART



STUDY CHARACTERISTICS

- 25 trials from 15 countries
- Europe 48%, Asia 28%, US 16%, others 8%
- 6 multicenter trials (smallest 3, largest 48)
- Largest study 1,082 patients (COLOR trial), smallest study 28 patients (Brazil)

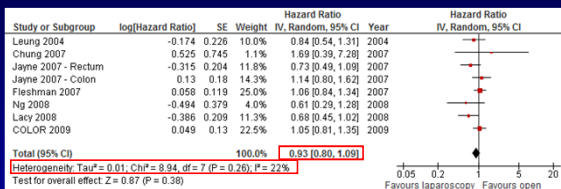
INCLUDED PATIENTS



- 4,279 patients with colon CA (66%), but none with transverse
- 2,209 patients with rectal CA (34%), but only 633 (9.8%) with low anterior resections

OVERALL SURVIVAL

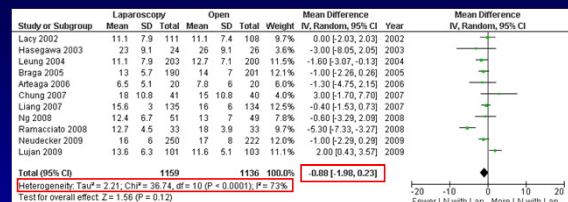
Only 7 trials provided sufficient data for pooling of HR



Colon only: HR 0.98 [0.83, 1.15], not heterogeneous

Rectum only: HR 0.70 [0.49, 1.00], p=0.05, not heterogeneous

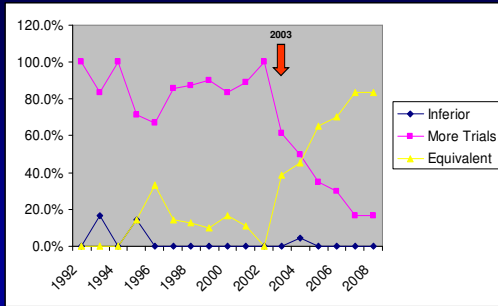
LYMPH NODE RETRIEVAL



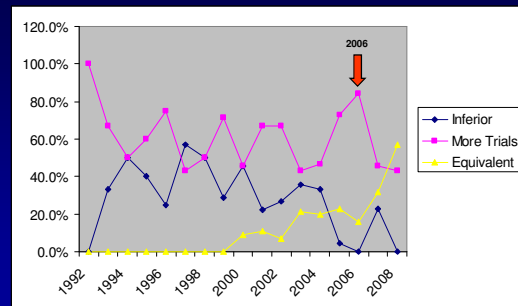
Colon only: mean difference -1.31 [-3.82, 1.20], significant heterogeneity

Rectum only: mean difference 0.08 [-1.69, 1.84], less heterogeneous

EXPERT OPINION – COLON CANCER



EXPERT OPINION – RECTAL CANCER



CONCLUSIONS

- Laparoscopy for colon cancer appears equivalent to open surgery in terms of major oncologic outcomes – it can be utilized in general practice
- There is currently insufficient RCT data to support the routine use of laparoscopy for rectal cancer – further trials are required
- Expert opinion in the literature is supportive of laparoscopy for colon cancer, particularly since 2003

FUNDING SOURCES



Canadian Institutes of Health Research



Canadian Association of Colon & Rectal Surgeons



Division of General Surgery / Department of Surgery
The Ottawa Hospital, University of Ottawa

Trials

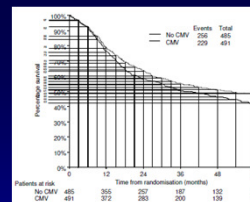
Methodology

Practical methods for incorporating summary time-to-event data into meta-analysis

Jayne F Tierney¹, Lesley A Stewart², Davina Ghersi³, Sarah Burdett¹ and Matthew R Sydes⁴

- Can calculate $\ln(\text{HR})$ and $\text{var}(\ln(\text{HR}))$ from published parameters (95%CI, p-value, randomization ratio)
- Can estimate from KM curve if parameters not provided
- Assumption that censoring is constant across time

Parmar 1998, *Statist Med*
Williamson 2002, *Statist Med*
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$$C_{0c}(t) = R_0(t) \left[\frac{1 - (t_0 - t_1)}{2(t_{max} - t_1)} \right] \text{ (assuming censoring at constant rate)}$$

$$R_{0c}(t) = R_0(t) - C_{0c}(t)$$

$$\ln(\text{HR}_c(t)) = \ln \left(\frac{D_{0c}(t)/R_{0c}(t)}{D_0(t)/R_0(t)} \right)$$

$$\text{var}[\ln(\text{HR}_c(t))] = \frac{1}{D_{0c}(t)} + \frac{1}{R_{0c}(t)} + \frac{1}{D_0(t)} + \frac{1}{R_0(t)}$$

Time at start of interval (months)	% Event-free on research	% Event-free on control	Reported numbers at risk on research	Reported numbers at risk on control
0	100	100	491	485
3	97	97	-	-
6	92	92	-	-
9	86	84	-	-
12	78	75	372	355
15	73	70	-	-
18	68	63	-	-
21	65	60	-	-
24	62	59	283	257
27	60	56	-	-
30	58	54	-	-
33	54	52	-	-
36	54	51	200	187
42	51	49	-	-
48	51	46	119	112
54	49	44	-	-
60	49	43	93	80

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