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UNIVERSITÀ DEGLI STUDI DI TORINO

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Long-term Oncologic Outcome After Laparoscopic Converted or Primary Open Resection for Colorectal Cancer: A Systematic Review of the Literature

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The author declares no conflicts of interest.

Abstract

Purpose: The aim of this study was to critically review the current evidence regarding the oncologic outcomes after laparoscopic converted or open resection for colorectal cancer.

Materials and Methods: A literature search was performed in Pubmed. Study selection and data acquisition were independently performed by 2 reviewers.

Results: The search strategy yielded a total of 746 articles, resulting in 7 studies eligible for inclusion. A total of 9190 (57 to 8307) patients were included in the open and 238 (17 to 56) in the converted group. In none of the studies, differences were found in disease stage between both groups. There were no significant differences between both groups with regard to overall survival, local recurrence and distant metastasis rate.

Conclusions: There is currently insufficient evidence that patients who had a laparoscopic resection for colorectal cancer converted to open surgery have a worse oncologic outcome than patients who were primarily treated by an open approach.

Laparoscopic colorectal cancer surgery has been introduced in the early 1990s and is increasingly applied since its introduction.1 Several randomized controlled trials (RCTs) have demonstrated short-term benefits of laparoscopy in colorectal cancer surgery and equivalent long-term oncologic outcome. However, a drawback of the laparoscopic approach in colorectal cancer surgery is the relatively high conversion rate of ~17% of patients.2,3

A recent review of the literature reported that conversion in laparoscopic colorectal cancer surgery seems to be associated with an adverse long-term oncologic outcome compared with patients who were successfully treated by laparoscopy.4 Moreover, it has been suggested by subgroup analysis that the oncologic outcome in converted patients is even worse compared with patients who were primarily operated on by an open approach.5 Most studies subjected to the oncologic outcome in converted patients in colorectal cancer surgery focus on the comparison with patients who were successfully treated by laparoscopy.6–8 However, several of these studies also included a cohort of patients who were primarily operated on by an open approach.9–15 Comparing the subgroups of converted and primarily open operated patients with regard to oncologic outcome would give the opportunity to find out whether conversion should be prevented, and the open approach should be preferred in the case preoperative doubt exists whether the operation could be successfully completed by laparoscopy or not. Moreover, most of these studies included a small patient population due to the fact that conversion is only necessary in a relatively limited number of patients, combining the outcomes of the different cohorts contributes to determine whether conversion negatively influences the long-term oncologic outcome compared with primary open

surgery or not.

The aim of this study was to summarize the current evidence with regard to the long-term oncologic outcome in patients who had a laparoscopic converted resection for colorectal cancer compared with patients who were primarily treated by an open approach.

Key Words: colorectal neoplasms; laparoscopy; conversion; survival

MATERIALS AND METHODS

A review of the literature was conducted according to the preferred reporting items for systematic reviews and meta-analysis.16

Search Stategy

A search strategy of the literature was independently performed by 2 reviewers (E.J.B.F. and M.E.A.) in MEDLINE, using the Pubmed search engine. The following search terms in title and abstract were used as free text words and medical subject headings: “colon,” “rectum,” “colorectal,” “rectal,” “conversion,” “cancer,” “laparoscopy,” and “laparoscopic.” The literature search was performed for all years, up to March 1, 2017.

Study Selection

The studies identified by the search strategy were subsequently selected based on title, abstract and full-text by 2 independent reviewers (E.J.B.F. and M.E.A.). Studies describing patients who underwent open or laparoscopic colon or rectal resection for cancer, and separately reported long-term outcome for the open and converted group were included. Prospective and retrospective cohort, and case-control studies were accepted as study design. Animal and non-English studies were excluded. Studies only reporting the short-term outcomes were also excluded.

Data Acquisition

Data of the included studies were independently acquired by 2 reviewers (E.J.B.F. and M.E.A.) using a standard data extraction form. The study design, number of total open and converted patients, sex ratio, age, body mass index, American Society of Anesthesiologists (ASA) score, location of the tumor, that is colon or rectum, and application of preoperative (chemo)radiation in rectal cancer patients were extracted from the individual studies. Collected intraoperative data included type of colorectal resection, conversion rate and reason for conversion. On the basis of the histologic assessment of the colorectal specimen, number of lymph nodes, presence of a positive resection margin and disease stage were extracted. With regard to long-term oncologic follow-up, time to follow-up, whether adjuvant chemotherapy was applied or not, local and distant recurrence rate, and overall as well as disease-free survival (DFS) were collected.

Assessment of Methodological Study Quality

The methodological quality of the included studies was assessed by the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses.17 Patient selection, comparability, and outcome are assessed in this score with a minimum of 0 points (poor methodological studies) and a maximum of 7 points for cohort studies (comparability not applicable) and a maximum of 9 points for case-control studies (excellent methodological quality). According to the methodological quality assessment, a level of evidence was assigned to the studies according to the Oxford Centre for Evidence-based Medicine Levels of Evidence.18 A Newcastle-

Ottawa assessment score <6 points was assigned as level of evidence 4 and a score of 6 or 7 points as 2B. Case-control studies were all assigned as level of evidence 3B.

Analysis

Data were analyzed using SPSS for Windows version 17.0 (SPSS Inc., Chicago, IL). Values were expressed as median (range). Statistical pooling of the data were not performed because of too much clinical heterogeneity between the included studies, that is location of the tumor throughout the colon and rectum, type of surgical procedure, tumor stage, and duration of reported survival rates.

RESULTS

The search strategy in MEDLINE yielded a total of 746 articles eligible for selection. On the basis of the inclusion and exclusion criteria, all articles were subsequently selected on title, abstract, and full-text (Fig. 1). Eventually, 7 studies were selected for inclusion in this review. This included 4 prospective 11–13,15 and 1 retrospective cohort studies,14 and 1 prospective 10 and 1 retrospective case-control study.9 The level of evidence was 2B in 1 study, 3B in 2 studies and 4 in the remaining 4 studies. In both case-control studies, the open and converted groups were matched for age, tumor location, and tumor stage. It was only reported in the study by Keller et al 13 what the reason was to primarily choose for an open resection (multivisceral resection, intraoperative radiotherapy, or surgeon's preference).

Three studies included colon and rectal cancer patients,9–11 2 12,13 only rectal and the remaining 2 studies 14,15 only colon cancer patients. Overall, a total number of 9190 (57 to 8307) patients were included in the group of patients who primarily underwent open colorectal cancer surgery and 238 (17 to 56) in the converted group. The baseline characteristics of the individual studies are reported in Table 1. There were no statistically significant differences found between both groups with regard to sex, age, and body mass index in any of the studies. In 2 studies, there was a significant difference with regard to ASA-score between both groups; in the study by Keller et al,13 patients with an ASA-score III were more frequently present in the open group (n=108, 70.8% vs. n=13, 52.0%; P=0.03), and in the study by Martínek et al 11 more ASA-score II patients were present in the converted group (n=102, 45.1% vs. n=13, 76.5%; P=0.039). Previous abdominal surgery rate was only reported in 2 studies. In the study by Bouvet et al 9 there was no significant difference between the open and converted group with regard to the number of patients who underwent previous surgery (n=22, 38.6% and n=18, 47.4%, respectively). However, there was a statistically significant difference between both groups in the study by Martínek et al 11 (n=105, 46.5% vs. n=3, 17.6%, respectively; P=0.018).

The type of colorectal resections performed in the individual studies is reported in Table 2, although this was not reported in 2 studies.10,15 In the study by Martínek et al 11 a large number of "other surgical procedures" was performed in the open group, including an intestinal bypass in 24 patients (10.6%) and diverting ileostomy or colostomy in 27 patients (11.9%). In the study by Keller et al 13 the "other surgical procedures" mainly included pelvic exenterations, in 42 patients (27.5%) in the open group and in 2 patients (8.0%) in the converted group. The application of (neo)adjuvant (chemo)radiotherapy was not significantly different between both groups in any of the studies (Table 2). The main reasons for conversion were tumor-related or anatomic-related reasons, intraoperative complications, or adhesions (Table 3).

Pathologic assessment of the specimen showed comparable rates of a positive resection margin between the open and converted group, reported in 4 of the 7 studies (Table 4). The number of lymph nodes harvested were similar in both groups in all studies, except in the study by Martínek et al 11 reporting a significantly higher number in the conversion group (13 vs. 11 lymph nodes, P=0.017). The disease stage of the patients in the individual studies are reported in

Table 4. In 2 studies,10,12 all disease stages, except stage IV were included. Martínek et al 11 included stages I to IV patients and in the studies by Li et al 14 and Ptok et al 15 only patients with stages I to III were included. In the remaining 2 studies, all disease stages (0 to IV) were included.9,13 There were no significant differences with regard to disease stage found between both groups in any of the studies.

Overall and DFS

The overall survival (OS) was reported in 6 studies (Fig. 2). In 2 of these studies, 3-year OS was reported,12,13 whereas 5-year OS was reported in the other studies.10,11,14,15 The OS was in favor of the open group in 4 studies 10,12,14,15 and in favor of the converted group in the other 2 studies.11,13 However, there was no statistically significant difference in OS between both groups in any of the studies.

DFS was reported in 6 studies (Fig. 3). In 1 study, 2-year DFS,9 in another study 3-year DFS 13 and in the remaining 4 studies 5-year DFS was reported.10,11,14,15 DFS was in favor of the converted group in 2 studies,11,13 although this did not reach statistical significance. In the other 4 studies,9,10,14,15 DFS was in favor of the open group. However, only in the study by Rottoli et al 10 this difference in DFS between both groups was statistically significant (63.3% vs. 40.2%, P=0.045).

Local and Distant Recurrence

The median duration of follow-up was 40 (26.0 to 75.0) months in the open group and 34.2 (26.0 to 66.0) months in the converted group. Duration of follow-up in the individual studies is reported in Table 1. Local recurrence rate was reported in 5 studies (Fig. 4). The local recurrence rate was in favor of the open group in 3 studies 10,11,14 and in favor of the converted group in the other 2 studies.12,13 However, there were no significant differences in local recurrence rate between both groups in any of the studies.

The rate of distant metastasis in the individual studies is depicted in Figure 5. The rate of distant metastasis was higher in the open group in all studies, except in the study by Rottoli et al 10 reporting a higher rate in the converted group. However, a significant difference in distant metastasis rate between both groups was present in none of the studies.

DISCUSSION

This review of the literature comparing the long-term oncologic outcome in converted patients and patients who were primarily treated by an open approach for colorectal cancer, show that there were no significant differences in OS and local and distant recurrence rate between both groups. Only 1 study reported a (borderline) significant difference in DFS in favor of the open group.

Subgroup analysis of the converted group of patients in the RCT by Jayne et al 5 comparing open and laparoscopic colorectal cancer surgery, showed a worse long-term oncologic outcome with regard to the OS in the group of patients who were converted. This finding might have led to the opinion of colorectal surgeons that the decision with regard to the approach, that is by laparoscopy or open surgery, should be made preoperatively to prevent a worse long-term oncologic outcome in the case conversion is necessary. In addition, this could also question whether the open approach should be preferred as the initial approach if any doubt exists whether the colorectal resection can be successfully completed by laparoscopy. Obviously, this decision should be made preoperatively on patient's factors and findings on preoperative imaging, for example, in patients with a bulky rectal tumor in a small (male) pelvis, local invasion of adjacent anatomical structures or extensive previous abdominal surgery harboring a high risk of intra-abdominal adhesions. This, however, might lead to the risk that primary open surgery is chosen in certain patients whereas it seems

intraoperatively that laparoscopic resection would have been feasible, hereby withholding this particular patient the short-term advantages of the laparoscopic approach. However, in none of the 7 studies included in this review the finding of the RCT was confirmed as there was no significant difference in OS between the open and converted group in any of the studies. There was only 1 study 10 reporting a significant difference between the open and converted group in DFS. However, this difference just reached statistical significance with a borderline P-value of 0.045.

Comparing the open and converted group of patients in colorectal cancer surgery is uncommon in most studies. The majority of authors only compare the converted patients with the group of patients in whom resection was successfully completed by laparoscopy. Although it is important to know the difference between these 2 groups in terms of long-term oncologic prognosis, the outcome of this analysis will not change clinical decision-making with regard to the approach chosen. The main reason most authors do not compare the open and converted group of patients is based on the argument that both groups are not comparable due to the fact that there must have been a certain reason why it was decided to choose the open approach, that is selection bias is probably present in the open group. However, this review showed that there were no differences between the open and converted group of patients with regard to baseline characteristics, including sex, body mass index, or age in any of the individual studies. In addition, the disease stage of the colorectal cancer was also not significantly different between both groups. Furthermore, in most of the studies considered in this review, consecutive patients were included during a certain time period, although the open group was matched to the converted group based on the abovementioned items in 2 studies.9,10

The overall and DFS was comparable among the studies reporting 5-year survival. The studies reporting a shorter survival period (2 or 3 y) reported higher survival rates. However, Keller et al 13 reported extremely high 3-year overall (>99% in both groups) and DFS rates. This is especially striking as a significant number of patients with stage IV colorectal cancer were included in this study as well. With regard to local recurrence, Li et al 14 reported an extremely high local recurrence rate (16.9% in the open group and 18.2% in the converted group) compared with the other studies, whereas the overall and DFS rates in this study were similar. A clear explanation for this finding is not given by the authors in this study. In addition, some studies reported a (nonsignificant) favorable survival or recurrence rate in the open group, whereas this was the case in the converted group in the other studies. So, inconsistency with regard to long-term oncologic follow-up was apparently present in the different studies included in this review, indicating that an evident preference for the open or converted approach in colorectal cancer surgery is lacking.

This review has some drawbacks, mainly due to the quality of the included studies. Clinical heterogeneity was obviously present as both colon and rectal cancer patients were included in almost half of the individual studies, and the surgical procedures were also considerably diverse, even including intestinal bypasses and diverting stomas for nonresectable cancers. In addition, there was also diversity in disease stage of the included patients as in some studies colorectal resections for benign lesions (stage 0) were included and in other studies patients with distant metastasis (stage IV). This is quite remarkable as one of the main outcome parameter of these studies was survival. It should have been more useful to only include patients with disease stages I to III. Furthermore, another disadvantage was the small number of patients included in the individual studies, especially the group of converted patients was relatively small in most studies.

In conclusion, there is currently insufficient evidence that patients who had a laparoscopic resection for colorectal cancer converted to open surgery have a worse oncologic outcome than patients who were primarily treated by an open approach. According to this finding, it should be preferred to start colorectal cancer surgery by laparoscopy and decide intraoperatively whether the resection can be completed by laparoscopy or conversion to an open approach is required.

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GALLERIA IMMAGINI

Figure 1

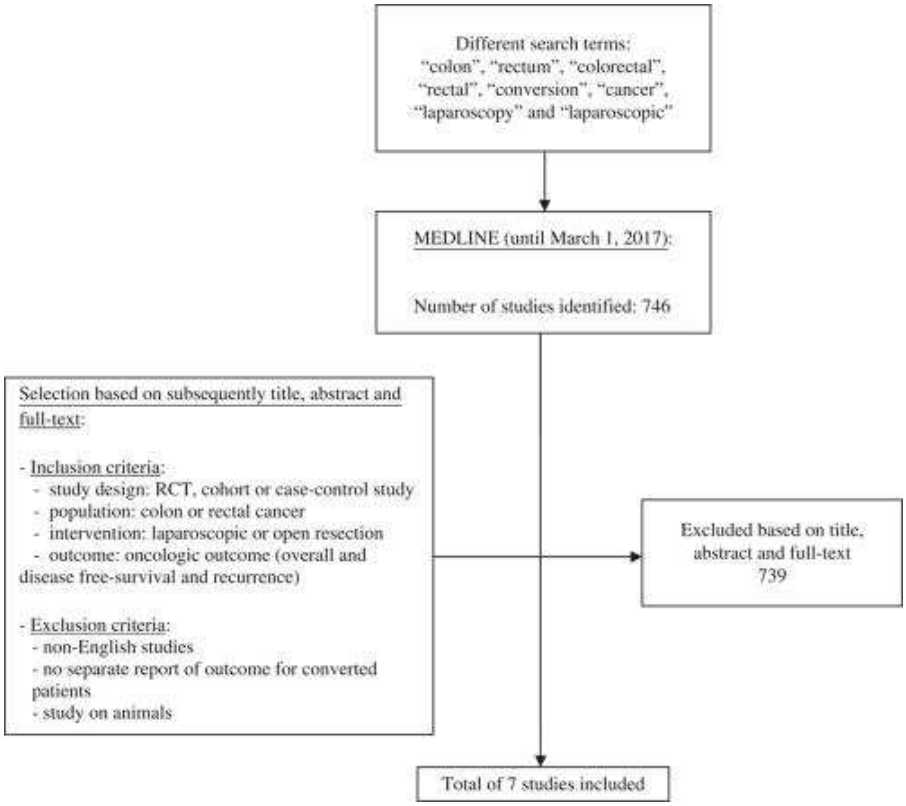

Table 1

References	Study Design	Newcastle-Ottawa Assessment Score	Level of Evidence	Colon and/or Rectal	Conversion Rate [n/N (%)]	No. Patients OPEN	
Bouvet et al[9]	Retrospective*	6	3B	Both	38/91 (41.8)	57 (60.0)	3
Rottoli et al[10]	Prospective*	5	3B	Both	NR	155 (83.3)	3
Martinek et al[11]	Prospective	5	4	Both	17/243 (7.0)	226 (93.0)	1
Rickert et al[12]	Prospective	5	4	Rectal	38/162 (23.5)	114 (75.0)	3
Kellice et al[13]	Prospective	6	2B	Rectal	25/141 (17.7)	153 (86.0)	2
Li et al[14]	Retrospective	4	4	Colon	33/217 (15.2)	178 (84.4)	3
Ptok et al[15]	Prospective	5	4	Colon	56/346 (16.2)	8307 (99.3)	5

*Case-control studies, the other studies were cohort studies.
ASA indicates American Society of Anesthesiologists; CONV, converted group; NA, not applicable; NR, not reported; OPEN, open group.

Table 2

References	Neoadjuvant Chemoradiotherapy [n (%)]		Type of Resection [n (%)]					
			Right Hemicolectomy		Left Hemicolectomy		Sigmoid Colon Resecti	
	OPEN	CONV	OPEN	CONV	OPEN	CONV	OPEN	CONV
Bouvet et al[9]	8 (80.0)*	5 (50.0)*	33 (57.9)	18 (47.4)	3 (5.3)	1 (2.6)	10 (17.5)	7 (18.4
Martinek et al[11]	NR	NR	45 (19.9)	3 (17.6)	16 (7.1)	2 (11.8)	41 (18.1)	3 (17.6
Rickert et al[12]	62 (54.5)	22 (57.9)	NA	NA	NA	NA	NA	NA
Keller et al[13]	112 (73.2)	19 (76.0)	NA	NA	NA	NA	NA	NA
Li et al[14]	NA	NA	69 (38.8)	12 (36.4)	53 (29.8)	10 (30.3)	56 (31.4)	11 (33.3

The studies by Rottoli et al[10] and Ptok et al[15] are not indicated as none of the items in this table were reported in their studies.
*Percentage of the total number of rectal cancer patients.
CONV indicates converted group; NA, not applicable; NR, not reported; OPEN, open group.

Table 3

References	n (%)				
	Tumor Related	Anatomic Related	Intraoperative Complication	Adhesions	Other Reas
Bouvet et al[9]	6 (15.8)	10 (26.3)	2 (5.3)	12 (31.6)	8 (21.1)
Rottoli et al[10]	12 (38.7)	6 (19.3)	2 (6.5)	11 (35.5)	0
Martinek et al[11]	3 (17.6)	6 (35.3)	5 (29.4)	0	3 (17.6)
Rickert et al[12]	7 (18.4)	11 (28.9)	4 (10.5)	6 (15.8)	10 (26.3)
Li et al[14]	15 (45.5)	4 (12.1)	4 (12.1)	10 (30.3)	0
Ptok et al[15]	15 (26.8)	8 (14.3)	7 (12.5)	9 (16.1)	17 (30.4)

The study by Keller et al[13] is not indicated as the reasons for conversion were not reported in this study.

Table 4

References	Positive Resection Margin [n (%)]		No. Lymph Nodes Harvested (%)		Disease Stage [n (%)]			
					Stage 0		Stage I	
	OPEN	CONV	OPEN	CONV	OPEN	CONV	OPEN	CONV
Bouvet et al[9]	0	0	10.0	9.0	2 (3.5)	4 (10.5)	20 (35.1)	7 (18.4
Rottoli et al[10]	6 (5.0)	1 (4.3)	22.0	22.4	OPEN: 9 (29.0); CONV: 58 (37.4)†			
Martinek et al[11]	1 (0.4)	0	11.0*	13.0	0	0	32 (14.2)	1 (5.9)
Rickert et al[12]	3 (2.6)	1 (2.6)	13.0	12.5	10 (8.8)	4 (10.5)	14 (12.3)	5 (13.2
Keller et al[13]	NR	NR	18.9	18.6	25 (16.3)	4 (16.0)	25 (16.3)	7 (28.0
Li et al[14]	NR	NR	19.3	17.6	0	0	16 (9.0)	3 (9.1)
Ptok et al[15]	NR	NR	NR	NR	0	0	1994 (24.0)	19 (33.9

†Stage 0 and I together.
CONV indicates converted group; NR, not reported; OPEN, open group.
*P-value of difference between OPEN and CONV is < 0.05.

Figure 2

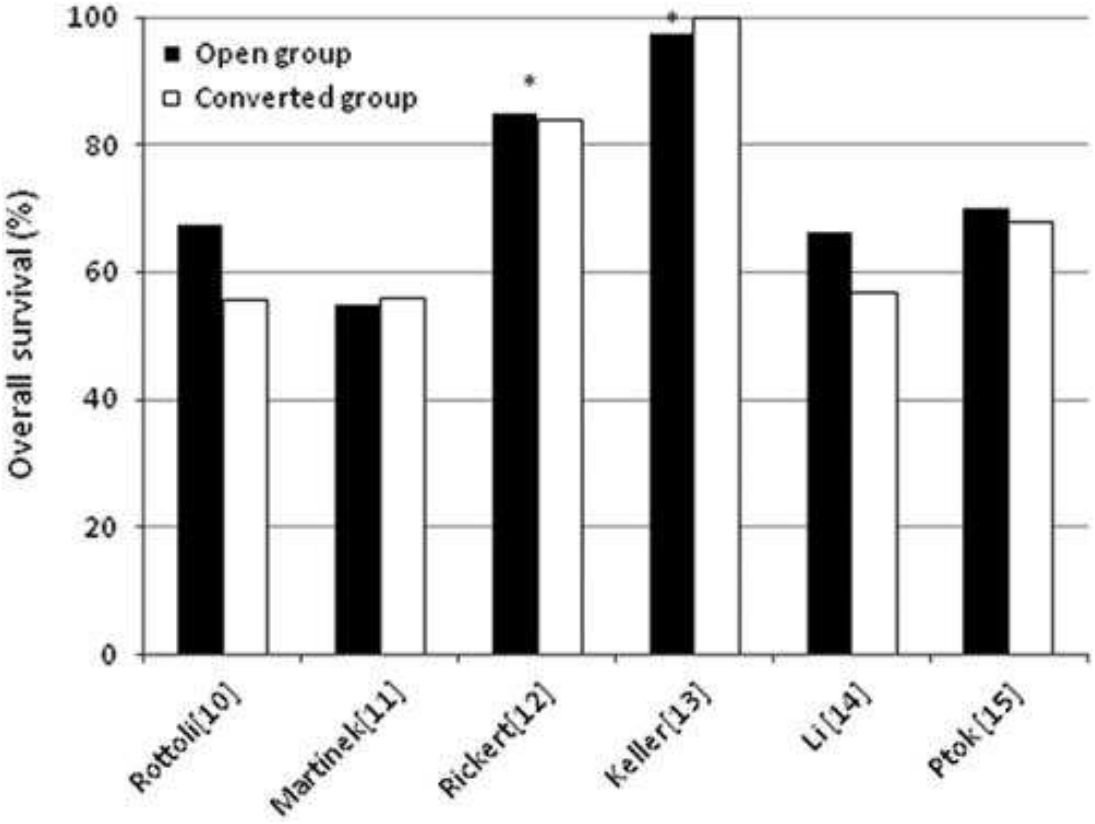
100
80
60
40
20
0
Overall survival (%)
Open group
Converted group
*
*
Rottoli[10]
Martinek[11]
Rickert[12]
Keller[13]
Li[14]
Ptok[15]

Figure 3

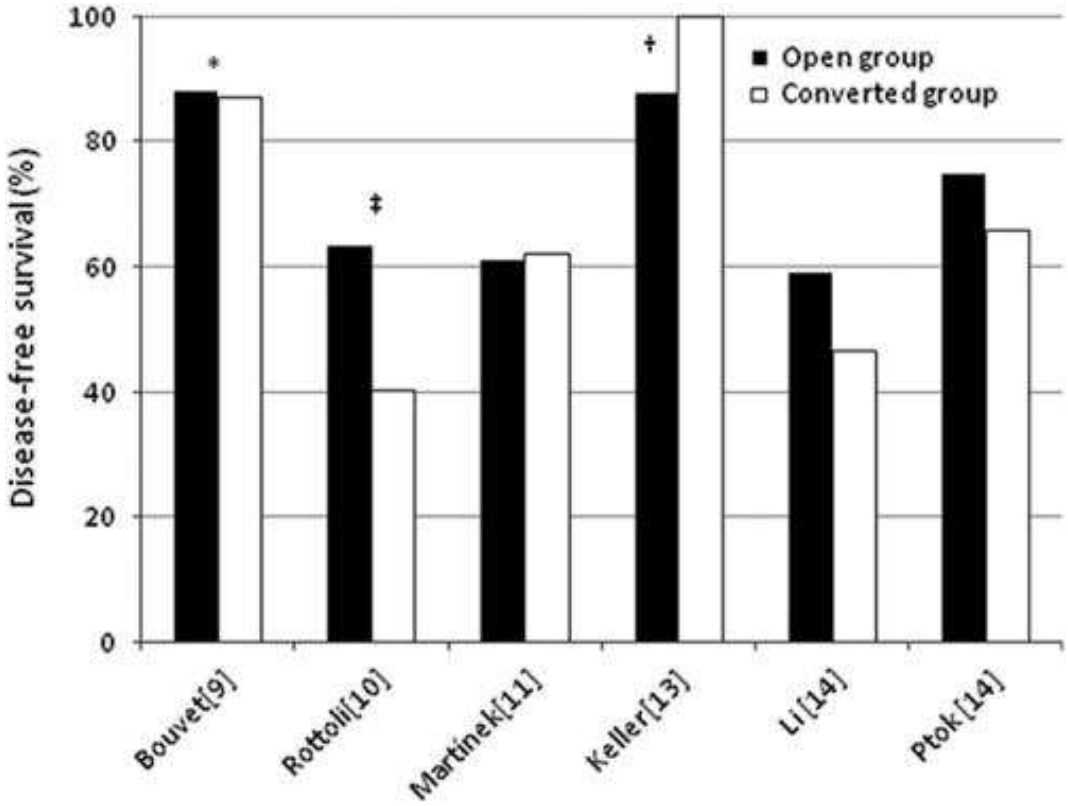
100
80
60
40
20
0
Disease-free survival (%)
*
‡
†
Open group
Converted group
Bouvet[9]
Rottoli[10]
Martinek[11]
Keller[13]
Li[14]
Ptok[14]

Figure 4

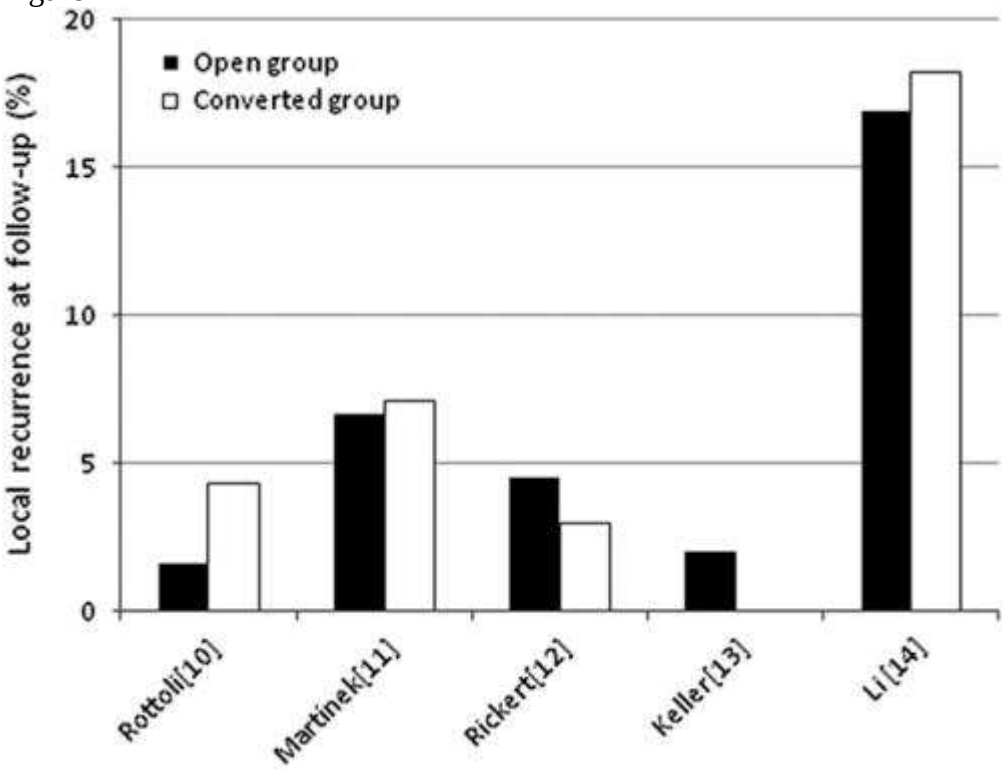

Figure 5