

REVIEW

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A Systematic Review on Overall Survival and Disease-Free Survival Following Total Pelvic Exenteration

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Abstract

Backgrounds: Total Pelvic Exenteration (TPE) is a radical operation for malignancies in which all of the organs inside the pelvic cavity, including the female reproductive organs, the lower urinary tract, and a part of the rectosigmoid are removed. In this study, we aimed to conduct a systematic review to assess the overall survival (OS) and disease-free survival (DFS) following TPE. **Methods:** This systematic review is composed of a comprehensive review of PubMed and Scopus databases with various related keywords to synthesis the overall survival and disease-free survival following TPE. The Synthesis Without Meta-analysis guideline was used to summarize the results. **Results:** We included the results of 39 primary studies and the results revealed that one-year OS of gynecological cancer in patients who have undergone TPE ranged from 50.0% to 72.0% and the 5-years OS ranged from 6.0% to 64.6%. The one-year survival rate of colorectal cancer patients was reported to be over 80% in almost all studies. The 3-year survival rate of patients varied from 25% to 75% and the lowest 5-year survival rate was 8% and the highest survival rate was 92%. To synthesis the disease-free survival rate in colorectal cancer, ten studies were included and one-year recurrence rate was 9.1% and the one-year DFS was reported as 61.0%. Three-year recurrence rate study was 20.4% and 3 and 5-year DFS ranged from 22.0% to 78.0%. **Conclusions:** The results suggested that DFS in primary advanced cancers is higher than locally recurrence tumors. This review showed that patient overall survival and disease-free survival rates have increased over time, especially at high volume centers that are more experienced and possibly better equipped. Therefore, it can be suggested that the attitude towards PE as a palliative surgery can be turned into curative surgery.

Keywords: Overall survival- disease- free survival- recurrence rate- total pelvic exenteration

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Introduction

Cancer is a major cause of death and one of the main barriers to increasing life expectancy in the world, and according to the World Health Organization, it is the first or second leading cause of death before the age of 70 in 121 countries, and its burden is rising rapidly worldwide (Bray et al., 2021; Sung et al., 2021).

Total Pelvic Exenteration (TPE) is a radical operation for malignancies and it is performed by an interdisciplinary team (Brunschwig, 1948; Yang et al., 2015). Brunschwig first presented this surgical procedure in 1948 (Brunschwig, 1948). In TPE surgery, all of the organs inside the pelvic cavity, including the female reproductive organs, the lower urinary tract, and a part of the rectosigmoid are removed (Vermaas et al., 2007; Ferenschild et al., 2009). This

technique is generally used in advanced gynecological cancers, as well as recurrent rectal cancer, comprising primary advanced and recurrent diseases (Shaikh et al., 2021) provided that both gynecological and rectosigmoid cancers are common in the world (Sung et al., 2021) and some of these patients would suffer from advanced conditions or recurrence, so they will demand a more advanced therapeutic approach like TPE.

Although it is an aggressive method, it seems to be the best choice for treating recurrent or advanced cancer patients with extensive pelvic disease (Berek et al., 2005). In recurrent or advanced cancer patients, TPE is the last resort therapeutic choice (as a salvage procedure) which can improve patients' survival (Berek et al., 2005; de Wilt et al., 2007).

Unlike the early years of introducing this technique, in

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recent years, the patients' survival, disease-free survival and mortality rate following this surgical procedure has improved. One-year and 5-year survival rate for patients with cervical, vaginal and uterine cancer was more than 70 and 50 percent, respectively (Berek et al., 2005; de Wilt et al., 2007) following TPE, in spite of the survival and mortality rate, the reported morbidity is still high (Chiantera et al., 2014; Vigneswaran et al., 2021).

The results obtained from different studies show that after TPE, the survival and mortality rate has been on the rise in the recent years. The reported results from countries and centers are different, mainly due to different experiences, equipment and the quality of postoperative care in each center. In this study, we aimed to conduct a systematic review to assess the overall survival and disease-free survival following TPE.

Materials and Methods

Study design

This systematic review is composed of a comprehensive review of two electronic international databases with various related keywords to synthesis the overall survival and disease-free survival in patients who had underwent TPE surgery because of primary advanced and recurrent cancers in the lower pelvic region. To prepare the report, we followed the reporting guideline of The Synthesis Without Meta-analysis (SWiM) presented by Campbell M. et al. (Campbell et al., 2020) and PRISMA Checklist (Page et al., 2021).

Search strategy

We searched the two international databases including Medline (via PubMed) and Scopus. To find the gray literature and additional primary studies, Google Scholar searched and the references list of retrieved publications manually searched. All English full-text primary studies published up to April 2021 were included in this review. Prospective or retrospective cohort studies were eligible to include. Patients with primary advanced or recurrent gynecological or rectosigmoid cancers were the target population and disease-free survival and 1, 3 or 5-year survival were extracted. To search the mentioned databases, a combination of keywords and Medical Subject Heading (MeSH) used, which included the following: Survival, mortality, Disease-Free Survival, Survival Analysis, Survival Rate, Pelvic Exenteration and Total Pelvic Exenteration filtered on human studies and English full-text studies. The search strategy is presented in Table S1 (Supplementary file).

Screening process

To screen the retrieved studies, all papers were included in the Endnote software. At first, duplicate papers identified and removed. Then, all remaining papers screened by title and abstract and irrelevant papers excluded. Finally, the full-text of remained papers was checked and all eligible papers with relevant data were included in the systematic review. Screening of articles done by two authors (AAH and MSF).

Data extraction

All relevant data extracted by two authors. To clean and manage the data, the extracted data entered into Excel software. The extracted data included title, the name of the first author of the article, year of publication, study duration, country of study, sample size, type of cancer, overall survival and disease-free survival of patients.

Grouping studies for synthesis

The retrieved studies differed in the type of cancer and the reported outcomes (i.e. mortality rate, overall survival and disease-free survival). Since all of the included articles did not report overall survival and disease-free survival rigorously and to reduce heterogeneity between studies, we grouped the articles according to the type of cancer (gynecological cancers and rectosigmoid cancers).

Synthesis methods

Because of different effect sizes reported in primary studies, and since in most cases the median survival reported along with interquartile range (IQR) instead of 95% confidence interval, meta-analysis was not possible. Summarizing effect estimates as a synthesis method used to summarize the obtained results. In this regard, we provided the minimum and maximum of overall and disease-free survival rate following TPE based on cancer type.

Criteria used to priorities results for summary and synthesis

We synthesis the results of studies based on reported outcomes and cancer site. In addition, we tried to assess the time trend of interested outcomes.

Investigation of heterogeneity in reported effects

To investigate heterogeneity in the findings, informal method used. In this method, we ordered the tables by hypothesized modifiers such as cancer type. In addition, the studies in tables was ordered by year, since it seems that time is a modifying factor and survival rates have been on the rise over time.

Certainty of evidence

In the included studies, 95% confidence interval was not reported; therefore, we tried other methods to examine the certainty of evidence such as the number of included studies and participants, the consistency of effect sizes and the risk of bias of the studies. To assess the risk of bias across studies, cohort adopted Newcastle Ottawa Scale (NOS) used which score ranged from 0 to 9 and the studies categorized in terms of study quality in the three groups as low (less than 3), moderate (3 to 6) and high (more than 6).

Data presentation methods and reporting results

We draw table to present the study findings to simplify the comparison. Sample size and risk of bias of the included studies were reported in the table and narrative text, because they might affect the interpretation of the results.

Limitations of the synthesis

One of the important limitations of data synthesis was the impossibility of performing meta-analysis for the following reasons. Studies had been conducted on different cancers, and the study populations were not the same. In some cases, outcomes were not reported by type of cancer. Required information such as effect size and variance (or 95% confidence interval) was not reported in most studies, which forced us to synthesize studies using summarizing effect estimates.

Results

Study selection

In this systematic review, 1506 primary studies (646 papers via Medline, 841 via Scopus and 19 papers via additional search) retrieved. Of the total articles, 573 duplicate articles were identified and removed. Then, the titles and abstracts of the remaining 933 articles were screened and at this stage, 635 articles were excluded due to the lack of fulfilling the inclusion criteria and the full text of 298 remained articles was evaluated, of which 39 articles entered into this systematic review and 259 studies

were excluded. All the process was presented in Figure 1.

Study characteristics

Thirty-nine studies published between 1967 and 2020 with total sample size of 2028 cases ranged from 9 to 232 were included in this review. Most studies have been done in the United States (with 11 studies) and no studies have been reported from Africa. In terms of cancer type, there were both primary and recurrent cancers among the studies and gastrointestinal (including: anus, rectum, colon, rectosigmoid and Soft tissue sarcoma), gynecological cancers (including: cervix, uterine, endometrium, vagina, ovary, vulva, leiomyosarcomas) and urologic cancers (bladder, urethra, prostate) were investigated. Some studies were designed only for gynecological cancers and some for gastrointestinal cancers. In some studies, both gynecological and gastrointestinal cancers were included, in which the outcomes were reported separately and, in some cases, together.

Risk of bias in studies and Reporting biases

The quality of included studies was assessed by NOS scale; 22 studies were methodologically graded as high

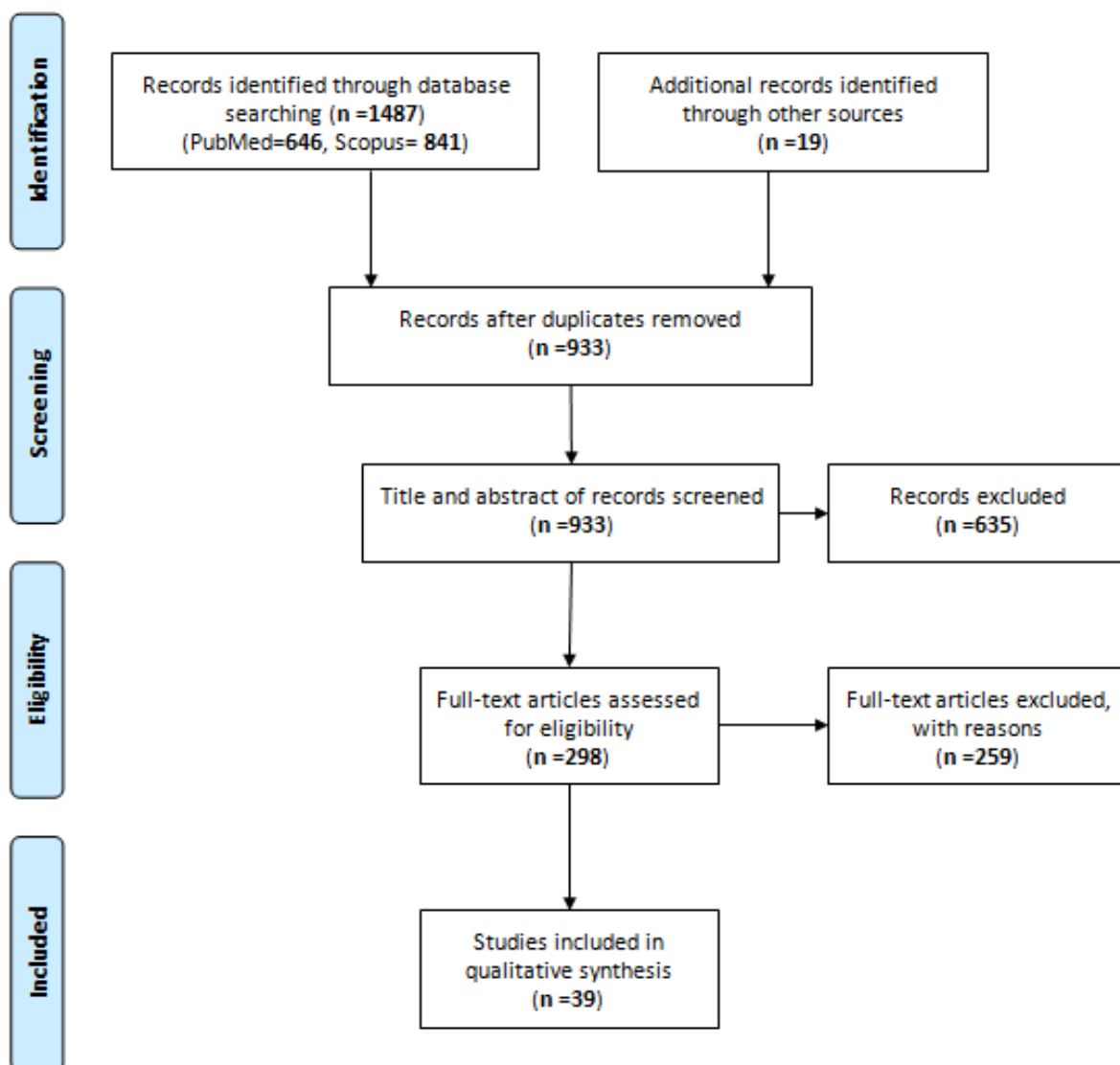


Figure 1. Flow Diagram of the Literature Search for Studies Included in the Systematic Review

Table 1. Overall Survival Rate Following Total Pelvic Exenteration by Cancer Type

Cancer type	First author	Year	Country	Primary tumor site	Sample size	OS rate	NOS
Gynecologic cancer	(Lewandowska et al., 2020)	2020	Poland	Recurrent Cervical Cancer	22	Median survival time: 11.5 IQR: (5-17.1) months	High
	(Nedyalkov et al., 2019)	2019	Bulgaria	Cervical cancer	9	*Approximately 1 year OS: 50%	Moderate
	(Seagle et al., 2016)	2016	The USA	Uterine cancer	60	Median OS: 37.4 95%CI: (20.2-71.2)	High
	(Guimarães et al., 2011)	2011	Brazil	Advanced gynecological cancer	13	2-year OS: 15.4%	Moderate
	(Kuhrt et al., 2012)	2012	The USA	Gynecologic (n=6), urologic malignancies (n=5), leiomyosarcomas (n=3), anal cancer (n=2), and benign disease (n=1).	17	The median survival: 6.9 months in the non-colorectal group	Moderate
	(Ferenschild et al., 2009)	2009	Netherlands	Cervical cancer (n=14), pelvic sarcoma (n=5), primary vagina carcinoma (n=1), and recurrent endometrial carcinoma (n=1).	21	5-year OS: Other cancer 45%. All patients with soft-tissue sarcoma were alive after 5 years.	High
	(Terán-Porcayo et al., 2006)	2006	Mexico	Cervical cancer	20	5-year OS: 64.6%	High
	(Goldberg et al., 2006)	2006	The USA	Gynecological and colorectal cancers (Cervical cancer (n=95), Endometrial cancer (n=2), Colon cancer (n=5 and Vulva cancer (n=1))	103	5-year OS: Cervical cancer: 48.4% All patients: 46.6.0%	Moderate
	(Sharma et al., 2005)	2005	The USA	Gynecological cancers	41	*3-year OS: 35.0% *5-year OS: 24.0%	High
	(Beitler et al., 1997)	1997	The USA	Cervix cancer	26	1-year OS: 72.0%* 3-year OS: 63.0%* 5-year OS: 63.0%	High
	(Lopez et al., 1994)	1994	The USA	Cervix (155), Rectosigmoid (27), Endometrium (16), Vagina (9), Bladder (5), Ovary (5), Anal (4), Vulva (4), Urethra (2), Prostate (2), Soft tissue sarcoma (2).	232	5-year OS: 42.0%	Moderate
	(Shingleton et al., 1989)	1989	The USA	Recurrent Cervical Cancer	78	1-year OS: 64.0%* 3-year OS: 44.0%* 5-year OS: 42.0% 10-year OS: 28.0%*	Moderate
	(Karlen and Piver, 1975)	1975	The USA	Gynecological cancer	29	2-year OS: 41.0% 3-year OS: 38.0% 5-year OS: 26.0%	Moderate
	(Ketcham et al., 1970)	1970	Georgia	UTERINE CERVIX	125	5-year OS: 34.0%	Moderate
	(Ingiulla and Cosmi, 1967)	1967	Italy	Advanced carcinoma of the cervix	105	5-year OS: 6.0%	Moderate
	Colorectal cancers	(Hagemans et al., 2018)	2018	The Netherlands	Rectal cancer	126	5-year: 44%
(Katory et al., 2017)		2017	The UK	Colorectal cancer	14	1 and 5-year: 92.9%	High
(Koda et al., 2016)		2016	Japan	Colorectal cancer	23	OS: 82.3% during a median follow-up period of 1258 days	High
(Nielsen et al., 2012)		2012	Denmark	Rectal cancer	90	3-year OS: * 62.0% for PARC 40.0% for LRRC 5-year OS: * 45.0% for PARC 20.0% for LRRC	High
(Kuhrt et al., 2012)		2012	The USA	Colorectal cancer group	36	The median survival: 21.4 months in the colorectal group	Moderate
(Mitulescu et al., 2011)		2011	Romania	Colorectal and non-colorectal	213	3-year OS: 67.0%* 5-year OS: 48.0%*	Moderate
(Domes et al., 2011)		2011	Canada	Locally advanced or recurrent rectal carcinoma	28	3-year OS: 75.1%	High
(Ferenschild et al., 2009)		2009	The Netherlands	Rectal cancer	48	5-year OS: Primary rectal: 66.0% Recurrent rectal: 8.0%	High
(Vermaas et al., 2007)		2007	The Netherlands	Primary locally advanced (n=23) and recurrent rectal cancer (n=12)	35	Primary locally advanced rectal cancer: 5-year OS: 52% Recurrent rectal cancer: 3-year OS: 32% 5-year OS: 16%	High
(Moriya et al., 2004)		2004	Japan	Recurrent Rectal Cancer	41	3-year OS: 58.0% 5-year OS: 40.0%.	Moderate
(Poletto et al., 2004)		2004	Brazil	Colorectal, anal, cervix, Vulva, Vagina, Endometrium, Urethra and Soft-tissue sarcoma	38	5-year OS: 41.2%	High

Table 1. Continued

Cancer type	First author	Year	Country	Primary tumor site	Sample size	OS rate	NOS
Colorectal cancers	(Kamat et al., 2003)	2003	The USA	Locally recurrent prostate cancer	14	1-year OS: 82.0%* 3-year OS: 58.0%* 5-year OS: 13.0%*	High
	(Ike et al., 2003)	2003	Japan	Primary Rectal Cancer	71	3-year OS: 68.0%* 5-year OS: 54.1% 10-year OS: 50.0%	High
	(Wiig et al., 2002)	2002	Norway	Advanced Primary and Recurrent Rectal Cancer	47	5-year OS: 28.0% Primary cancers: 36% Recurrent cancer: 18%	High
	(Law et al., 2000)	2000	Hong Kong	Primary or recurrent rectal cancer	24	5-year OS: 44.0% primary rectal cancer: 64.0%	High
	(Russo et al., 1999)	1999	The USA	Rectal cancer	47	1-year OS: 85.0%* 3-year OS: 34.0% 5-year OS: 20.0%*	High
	(Bramhall et al., 1999)	1999	The USA	Locally advanced pelvic tumors	50	1-year OS: 68.0% 5-year OS: 18.0%	High
	(Shirouzu et al., 1996)	1996	Japan	Locally advanced colorectal cancer	17	5 and 10-year OS: primary cancer/ stage II: 71.0% 3 and 5-year OS: recurrent cancer/curative surgery: 25.0%	Moderate
	(Luna-Perez, 1996)	1995	Mexico	Primary rectal adenocarcinoma	18	1-year OS: 88.0%* 3-year OS: 57.0%* 5-year OS: 57.0%	High
	(Liu et al., 1994)	1994	China	Advanced rectal carcinoma	31	5-year OS: 52.0% 5-year OS/Primary cancer: 56.0%	Moderate
	(Takagi et al., 1985)	1985	Japan	Advanced cancers of the rectum and distal sigmoid colon	13	5-year OS: 38.5%*	Moderate
(Boey et al., 1982)	1982	Hong Kong	Locally advanced colorectal cancer	26	5-year OS: 30.4%	Moderate	

*Estimated from Kaplan-Meier curve

Table 2. Disease Free Survival Rate Following Total Pelvic Exenteration by Cancer Type

Cancer type	First author	Year	Country	Primary tumor site	Sample size	DFS	NOS
Gynecologic cancer	(Park et al., 2007)	2007	Korea	Gynecologic cancers	30	Median DFS: 12.00 months, 95%CI= (4.50–19.50)	Moderate
Colorectal cancers	(Bogner et al., 2021)	2021	Germany	Colorectal cancer, gynecological malignancies, anal cancer, and other primary tumors	63	The recurrence-free survival: 9.3 (IQR 5.0–24.7) months.	High
	(Hagemans et al., 2018)	2018	The Netherlands	Rectal cancer (locally advanced rectal cancer and locally recurrent rectal cancer)	126	3 and 5-year Local RFS rates were 78% in elderly patients and in younger patients: 3-year LRFS: 65% and 5-year LRFS: 61%	High
	(Katory et al., 2017)	2017	The UK	Colorectal cancer	14	1 year recurrence: 9.1% 3-year recurrence: 20.4% 5-year recurrence: 33.7%	High
	(Koda et al., 2016)	2016	Japan	Colorectal cancer	23	5-year DFS: 71.8%	High
	(Nielsen et al., 2012)	2012	Denmark	Rectal cancer	90	3-year DFS: 42.3% (24.8–58.7) for PARC 22.0% (10.2–36.6) for LRRC 5-year DFS: 25.9% (11.4–43.2) for PARC 22.0% (10.2–36.6) for LRRC	High
	(Domes et al., 2011)	2011	Canada	Locally advanced or recurrent rectal carcinoma	28	3-year DFS: 52.2%	High
	(Poletto et al., 2004)	2004	Brazil	Colorectal, anal, cervix, Vulva, Vagina, Endometrium, Urethra and Soft-tissue sarcoma	38	5-year DFS: 37.8%	High
	(Chen and Sheen-Chen, 2001)	2001	Taiwan	Locally advanced primary colorectal cancer	50	5-year DFS: stage II primary disease: 62.0% stage III primary disease: 35.0%	Moderate
	(Luna-Perez et al., 1995)	1995	Mexico	Primary rectal adenocarcinoma	18	1-year DFS: 61.0%* 3-year DFS: 72.0%* 5-year DFS: 61.0%	High
(Boey et al., 1982)	1982	Hong Kong	Locally advanced colorectal cancer	26	5-year DFS: 22.2%	Moderate	

*Estimated from Kaplan-Meier curve

quality and 17 as medium standard.

Results of individual studies and syntheses

Overall Survival rate in gynecological cancer

Fourteen studies with 901 cases were included to summarize the overall survival rate in gynecological cancers following TPE. Different types of cancers such as cervical, uterine, endometrial, vaginal, ovarian and urethral were investigated. As it was shown in Table 1, the lowest sample size was 9 conducted by K. Nedyalkov et al. (Nedyalkov et al., 2019) and the highest was 232 cases by Lopez, M. J. et al. (Lopez et al., 1994) The newest and oldest studies were conducted in 2020 by Lewandowska, A. et al. (Lewandowska et al., 2020) and in 1970 by A. S. Ketcham et al. (Ketcham et al., 1970) respectively.

One-year OS ranged from 50.0% in a study conducted by K. Nedyalkov et al. (Nedyalkov et al., 2019) to 72.0% in J. J. Beitler et al. (Beitler et al., 1997) study which was carried out on cervical cancer patients. The 5-years OS ranged from 6.0% in a study conducted by Ingiulla, W. et al. (Ingiulla and Cosmi, 1967) on 105 patients with advanced carcinoma of the cervix in Italy, 1967 to 64.6% in 2006 on 20 cervical cancer patients in Mexico by M. A. Terán-Porcayo et al. (Terán-Porcayo et al., 2006) (Table 1).

Overall Survival rate in colorectal cancer

Twenty-two primary studies with totally 1050 patients were included in systematic review to summarize the overall survival rate in colorectal cancers following TPE. The newest study was conducted in the Netherlands, 2018 with 126 cases by J.A.W. Hagemans et al. (Hagemans et al., 2018) and the oldest in Hong Kong, 1982 with 26 cases by Boey, J. et al. (Boey et al., 1982).

The one-year survival rate of patients was reported to be over 80% in all studies, except for one article that was conducted by S. R. Bramhall et al. (Bramhall et al., 1999) in the USA, 1999, in which the one-year survival rate of patients with locally advanced pelvic tumors was reported to be 68%.

The 3-year survival rate of patients varied from 25% in the study of K Shirouzu et al., (Shirouzu et al., 1996) which was conducted in Japan, 1996 on recurrent cancer patients, to 75% in the study of Trustin S. Domes et al., (Domes et al., 2011) conducted on locally advanced or recurrent rectal carcinoma in Canada, 2011.

Regarding the 5-year survival rate, the lowest 5-year survival rate was 8% in the F. T. J. Ferenschild et al. (Ferenschild et al., 2009) study on recurrent rectal cancer patients in the Netherlands, 2009, and the highest survival rate was 92% in the study of Mark Katory et al. (Katory et al., 2017) in the UK, 2017 (Table 1).

Disease Free Survival rate in gynecological cancer

Only one study was carried out on gynecological cancers and reported disease-free survival, which was a study in Korea that reported a median survival time of 12 months. This study was conducted by Park, J. Y. et al. (Park et al., 2007) on 30 gynecologic cancers patients.

Disease-Free Survival rate in colorectal cancer

To summarize disease-free survival rate in colorectal cancer ten studies with 476 cases were included. One-year recurrence rate in Katory, M. et al. (Katory et al., 2017) study which was conducted on 14 colorectal cancer patients in UK, 2017 was 9.1% and the one-year DFS was reported as 61.0% in study by Luna-Perez, P. et al. (Luna-Perez et al., 1995) on primary rectal adenocarcinoma in 1995. Three-year recurrence rate in Katory, M. et al. (Katory et al., 2017) study was 20.4% and 3-year and 5-year DFS ranged from 22.0% to 78.0% in M. B. Nielsen et al. (Nielsen et al., 2012) study and J.A.W. Hagemans et al. (Hagemans et al., 2018) study, respectively. DFS in primary advanced cancers and stage II primary disease is higher than locally recurrent tumors and stage III primary disease.

Discussion

In this systematic review we summarized the overall and disease-free survival rates in patients who had undergone TPE. We included the results of 39 primary studies and the results revealed that one-year OS of gynecological cancer in patients who have undergone TPE ranged from 50.0% to 72.0% and the 5-years OS ranged from 6.0% to 64.6%. The one-year survival rate of colorectal cancer patients was reported to be over 80% in all studies, with the exception of one article conducted by S. R. Bramhall et al. (Bramhall et al., 1999) in USA, 1999, where the one-year survival rate of patients with locally advanced tumors was reported to be 68%. The 3-year survival rate of patients varied from 25% to 75% and the lowest 5-year survival rate was 8% and the highest survival rate was 92%.

Regarding disease-free survival in gynecological cancers, a study in Korea by Jeong-Yeol Park et al. (Park et al., 2007) on 30 gynecologic cancer patients reported a median survival time of 12 months. To synthesis the disease-free survival rate in colorectal cancer, ten studies were included and one-year recurrence rate in Katory M et al. (Katory et al., 2017) study was 9.1% and the one-year DFS was reported as 61.0% in study by P. Luna-Perez et al. (Luna-Perez et al., 1995) which was conducted on primary rectal adenocarcinoma in 1995. Three-year recurrence rate in Katory M et al. (Katory et al., 2017) study was 20.4% and 3 and 5-year DFS ranged from 22.0% to 78.0% in M. B. Nielsen et al. (Nielsen et al., 2012) study and J.A.W. Hagemans et al. (Hagemans et al., 2018) study, respectively. The results suggested that DFS in primary advanced cancers and stage II primary disease is higher than locally recurrence tumors and stage III primary disease.

The main indications for PE include primary, recurrence or locally advanced tumors (cervix, rectum, Vulva, bladder) and recurrence after radiotherapy (cervix) and sarcoma (Ethem Unal et al., 2019; PelvExCollaborative, 2019). While distant metastases include involvement of the iliac vessels, pelvic side wall and para-aortic lymphadenopathy, proximal of sacrum bone to S1/S2 or sciatic foramen are contraindications

(Ethem Unal et al., 2019).

Despite the morbidity of more than 50% , the complications of surgery up to 60% and surgical reoperation up to 10% of cases, the number of cases of complete PE is increasing in the world (Lewandowska et al., 2020). Anyway, recent studies tend to more radical surgeries including sidewalls and vessels and perhaps because of this, surgical indications are more common at this time (Ethem Unal et al., 2019; Lewandowska et al., 2020). However, the risk of surgical complications in TPE has been reported to be 31.6-86%. Also, the surgical morbidity for cases of locally advanced cancer is 47.1%, which is 82% in cases of recurrent cancer (Lewandowska et al., 2020; Bogner et al., 2021). The most common postoperative complications after TPE surgery include hemorrhage 31.8%, ileus 25.8%, wound complications 21.3% and respiratory failure 16.1%. the less common complications include sepsis, thromboembolism, heart failure, fistula and abscess (Lewandowska et al., 2020).

One of the most common and significant causes of surgical complications is radiotherapy as neoadjuvant therapy. Although radiotherapy increases the chances of a negative resection margins, but it has no effect on survival for either colorectal or non-colorectal cancer (Bogner et al., 2021). PE has been a revolution in recent years, and according to the studies, the 5-year survival rate in these patients raised up to 60%. Despite the improvement of OS, the complications of radical surgery are still high and margin status is the only significant factor in disease free survival (DFS). The mortality rate decreased from 4-7.2% in last decade to 1.9-2.3% in recent reports (Lewandowska et al., 2020) and the quality of life of patients increased (Brown et al., 2017; Lau et al., 2019).

However, TPE is an invasive procedure and the patients need double stomas for urinary and fecal excretion (Koda et al., 2016). But The opportunity to survive for a long time with less complications and better quality of life is achievable with TPE which is now performed at high volume centers and It is also an alternative method to increase the life expectancy of patients (Yang et al., 2013; Katory et al., 2017; Waters et al., 2019).

A review of the included studies showed that patient overall survival and disease-free survival rates have increased over time, and in high volume centers that are more experienced and possibly better equipped, survival rates are higher. On the other hand, the review of articles showed that in most centers, the sample size is very small and for better conclusions about the survival rate after TPE, a multicenter study with a large sample size and longer follow-up time is recommended.

In addition to the above, the review of the articles showed that in the majority of articles, different types of cancers have been stacked and analyzed, which requires specific studies for each cancer in order to achieve more accurate results.

Finally, more attention to analysis methods can be helpful in summarizing the results. Regarding survival analysis, reporting the survival rate for a specific time (1, 3, 5 years, etc.) with a 95% confidence interval is required for meta-analysis, which was not reported in most studies, and that is an important indicator for generalizing the

results of a study to other populations and also to measure the level of uncertainty in a sample variable.

Limitation

It is problematic to distinguish the overall survival and disease-free survival and their relationship with TPE, as primary studies combined diverse types of cancer and dissimilar modalities methods of pelvic exenteration. Most studies have not reported a confidence interval and therefore, meta-analysis was not possible in this study. And the sample size has been limited in most studies, so it is recommended to conduct studies with larger sample sizes to achieve more accurate results.

In conclusion, the results suggested that DFS in primary advanced cancers is higher than locally recurrence tumors. In summary, this review showed that patients' overall survival and disease-free survival rate have increased over time, especially when PE performed at high volume centers that are more experienced and possibly better equipped. Therefore, it can be suggested that the attitude towards PE as a palliative surgery can be turned into curative surgery.

Abbreviations

DFS: Disease free survival, TPE: Total Pelvic Exenteration, PE: Pelvic Exenteration, OS: Overall survival, MeSH: Medical Subject Headings, PRISMA: Preferred Reporting Items for Systematic Review and Meta-Analysis, SWiM: The Synthesis without Meta-analysis, NOS: Newcastle Ottawa Scale.

Author Contribution Statement

SRM, SA, AM, SRH, SS, AE and AAH conceived the study. All authors contributed to the title and full-text screening. AAH, AE and MSF extracted the data. All authors contributed equally to the initial draft of the manuscript. AAH, MSF, SRM and AE summarized the data and all authors have read and revised and approved the final version of the manuscript. Corresponding Author: Correspondence to Arezoo Esmailzadeh.

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Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

All data generated or analyzed during this study are included in this published article.

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Competing interests

All authors declared no conflict of interest.

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