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REVIEW

Primary retroperitoneal mucinous cystadenocarcinoma (PRMCa): a systematic review of the literature and meta-analysis

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Abstract
Purpose Primary retroperitoneal mucinous cystadenocarcinoma (PRMCa) is a rare tumour. Prognosis and optimal management are not well established. In view of a case managed in our Centre, we performed a systematic review and meta-analysis.
Method Systematic review of medical electronic databases for published data (1950–12/10/2015). No RCTs identified. Individual patient data detracted from case reports and case series were analysed
Results In total, 73 female and 5 male cases of PRMCa identified including our case. Median age at diagnosis was 42.0 years (range 18–86 years), with women being significantly younger than men at diagnosis (42.0 years versus 62.2 years, $p = 0.005$). A palpable abdominal mass and abdominal pain were the most common presentations in 42.9 and 23.8 % of cases, respectively. Twenty-six women were <38 years old. There were 16 women <38 years old that had surgical data reported, of which 14 underwent fertility-sparing surgery with excision of the mass. Adjuvant chemotherapy was given in 24.1 % (13/72) women. Follow-up ranged from 1 to 130 months with a median of 15 months. Of the 57 cases that had follow-up reported, recurrence occurred in 23 cases (40.4 %) within a median of 8 months from diagnosis. Median disease-free survival was 15 months (range 1–130 months). Of the women who recurred, 14 died of their disease giving 1, 2 and 5-year disease-specific survival rates of 85.9, 80.7 and 75.4 %, respectively.
Conclusion PRMCa are rare and potentially aggressive tumours that often occur in young women. Removal of the tumour, adequate staging and adjuvant chemotherapy needs to be considered.

Keywords Primary · Retroperitoneal · Mucinous cystadenocarcinoma · Prognosis · Treatment

Introduction

Mucinous adenocarcinomas are a common tumour type; however, development in the retroperitoneum, as the primary tumour site, is a rare occurrence [1, 2]. Histologically, primary retroperitoneal mucinous tumours (PRMTs) are of three types: mucinous cystadenomas, mucinous borderline tumours and mucinous cystadenocarcinomas. In view of a case of primary retroperitoneal mucinous adenocarcinoma, which has been treated in our centre, we performed a systematic review and a meta-analysis of published data.

Materials and methods

In order to understand the natural history and prognosis of this rare malignancy a systematic review of the literature was undertaken. Using the terms "primary" and

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"retroperitoneal" and "mucinous" and "cystadenocarcinoma" or "adenocarcinoma" contained in title and/or abstract and/or keywords, a systematic search was conducted through databases of Medline, EMBASE, EBSCO, CINAHL and Google Scholar (01/01/1950–10/10/2015) for published data. Borderline tumours, adenomas, other histological sub-types and metastasis to retroperitoneum were excluded. To ensure completeness, we cross-referenced our search results and hand-searched for additional titles. Using PRISMA flowchart [3] 53 papers were identified (Fig. 1). There was no Randomised Control Trial (RCT); only observational studies were identified with one case series and the rest being case reports. For non-English papers, we included data from the English published abstract. We crosschecked them with English published manuscripts that included these papers and collated individual patient data from results and tables. Two authors (EM and IL) independently performed literature research and data collection. Data collected included patient age at diagnosis, gender, symptoms on presentation, tumour size, surgical

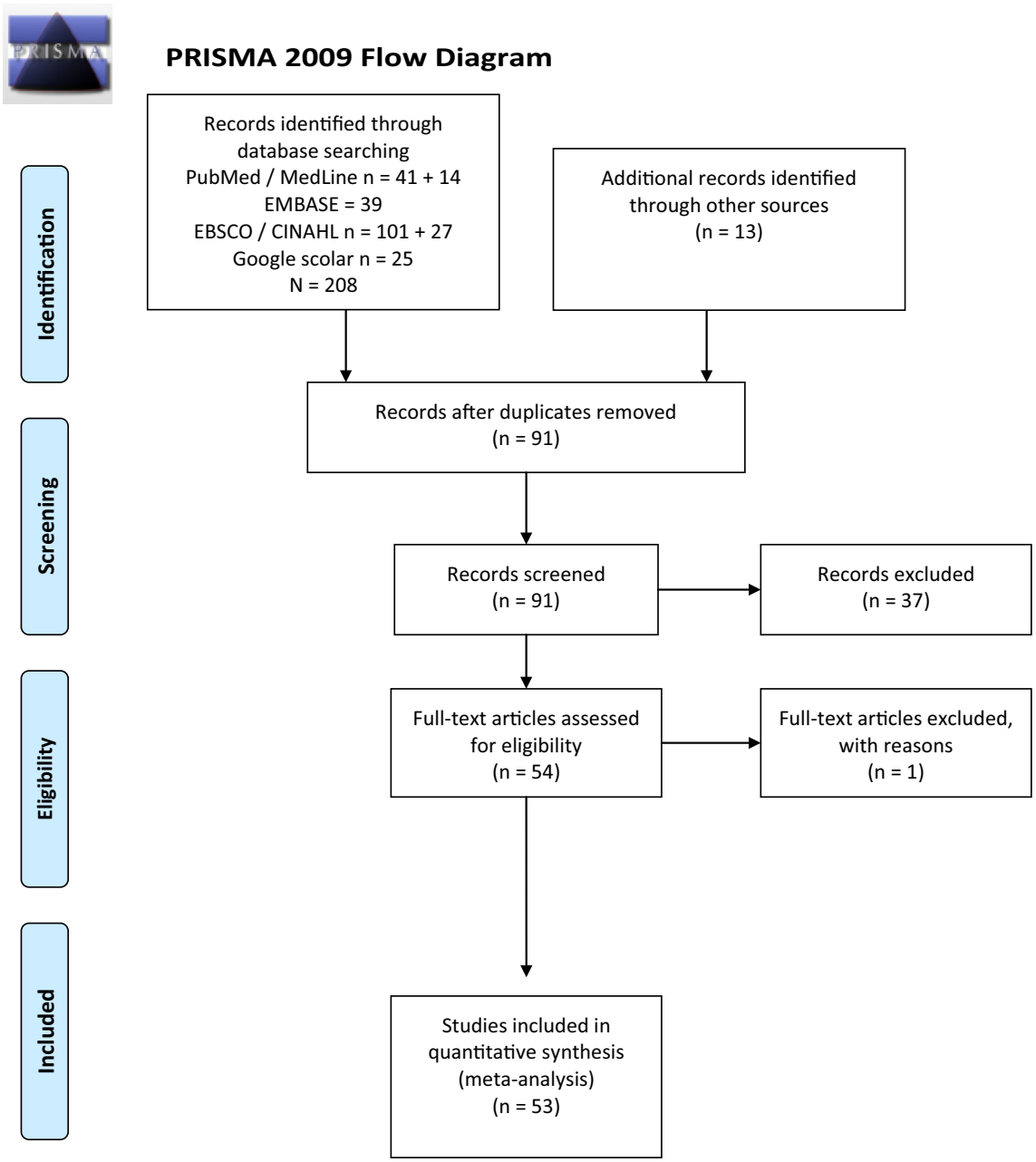

Fig. 1 PRISMA 2009 flow diagram. From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

and/or adjuvant treatment, follow-up, disease recurrence and survival. In the 53 selected publications, 77 cases of PRMCa have been reported. We performed a meta-analysis excluding the male cases, in order to determine the management and the impact on survival for these rare tumours on females. Although results of meta-analysis of case reports and series are not robust, however, in the absence of other RCT or observational studies, this seems the way forward to help clinical decisions [4, 5]. Since this meta-analysis is of case reports, we have included our case, described above (unpublished data).

For the meta-analysis, Microsoft Excel was used to collate the data and statistical evaluation performed using SPSS 22.0 (IBM). Descriptive statistics were used to analyse both continuous and categorical variables. Mean values with Standard Deviation (SD) and Standard Error (SE) of mean with Confidence Interval (CI) of 95 % were calculated. For normal distributions, t test was used, and for non-parametric distributions Kruskal–Wallis Test was used to compare median values and categorical characteristics among groups. Kaplan–Meier curves were plotted for survival and statistical significance value was considered with $p < 0.05$.

Results

The systematic review revealed 73 cases of primary retroperitoneal mucinous cystadenocarcinomas (PRMCa) reported in females, mainly as case reports and thirteen of them as part of small case series (Table 1). Five cases were reported in males. Males were significantly older at presentation with a median age of 62.2 years (SE 6.5) compared to a median of 42.0 years (SE 1.6) for the females ($p < 0.05$).

Details of clinical presentation were available in 42 of the 73 women. The majority, 18 of the 42 (42.9 %) presented with a palpable abdominal mass, 10 (23.8 %) presented with abdominal pain and 9 with abdominal distension (21.4 %). Only four patients (9.5 %) were asymptomatic at the time of diagnosis. Large tumour size was associated with abdominal distension and pain. The mean tumour diameter was 15.1 cm (SD 6.3, SE 0.8 cm) and 85.5 % of the masses were larger than 10 cm in maximum diameter on the histopathological examination.

Serum tumour marker levels were checked in 24 of the 77 cases. CA125 was elevated only in 3/18, CEA in 4/14 and CA19.9 in 5/13 cases. These results did not statistically correlate with the size of mass. Tumour markers level at the time of diagnosis did not have a prognostic significance for disease recurrence or survival.

Complete surgical excision of the retroperitoneal mass was the primary treatment in all cases. Unfortunately, data regarding tumour rupture during surgery or capsule involvement in the final histopathology was only recorded in 21 cases, of which five had capsule involvement or surgical rupture during removal. There was no significant difference in the recurrence rate between cases where the mass was removed intact and those where it was not, 63.6 versus 50 % ($p > 0.05$).

Twenty-six women were <38 years old, of which 16 women had surgical data reported and 14 of these (87.5 %) underwent fertility-sparing surgery with excision of the mass and preservation of the uterus and at least one ovary. There was no obvious survival benefit noted for those that underwent bilateral salpingo-oophorectomy (median survival 53.6 months (SE 4.2)) compared to those that did not (median survival 55.9 months (SE 7.1), $p = 0.173$).

Overall, only 24 % (13/54) of female patients received adjuvant chemotherapy. The commonly used chemotherapeutic regimes were Cyclophosphamide and Adriamycin (CA), Cyclophosphamide, Adriamycin and Cisplatin (CAP) or cisplatin alone (Table 2). Interestingly, 5/13 cases which were reported after 2007, received carboplatin alone or in combination with Paclitaxel. None received radiotherapy and one patient was treated with Tamoxifen when diagnosed with recurrent disease as palliative treatment.

Of the 13 women who received adjuvant chemotherapy, 11 had survival data reported and of these five died (45.4 %). In comparison, for women who did not receive adjuvant chemotherapy 5/41 (12.2 %) did not survive, however, there was no statistically significant difference in the characteristics of the two groups (age, tumour size and surgical treatment) ($p > 0.05$).

Follow-up was reported in 57 out of 73 female cases, ranging from 1 to 130 months, with a median follow-up of 15 months. During the follow-up period, 23 recurrences (40.4 %) and 14 deaths (24.6 %) were reported giving overall 1, 2 and 5-year survival rates of 85.9, 80.7 and 75.4 %, respectively. Median time from diagnosis to recurrence was 8 months (range 1–58 months) (Figs. 2, 3).

Discussion

The first reported cases of PRMCa were in 1976 by Roth [6]. Since then there have been a further 75 cases reported in the literature. This systematic review and meta-analysis of these cases show that PRMCa are most commonly observed in premenopausal women and usually present with abdominal pain and a palpable mass that is thought to be of pelvic or ovarian origin. Differential diagnosis in cases where malignancy and retroperitoneal location has been identified pre-operatively includes metastases from intraperitoneal organs for example ovaries, gastrointestinal

Table 1 Primary retroperitoneal mucinous cystadenocarcinoma cases reported in literature, $n = 78$

References	Age (years)	Gender	Presenting symptom	Size, max. diameter (cm)	Surgical treatment in addition to tumour resection	Mass removal	Chemo therapy	Recurrence	DFS	Recurrence site	OS	Status
Douglas et al. [19]	18	F	N/R	5	Mass excision only	N/R	Yes	Yes	N/R	N/R	N/R	DOD
Tykka et al. [20]	23	F	N/R	10	Mass excision only	ruptured	No	Yes	1	Colon	11	DOD
Roth et al. [4]	48	F	Abdominal distension	N/R	N/R	N/R	No	Yes	6	Lung, liver	6	DOD
Tamura et al. [21]	51	F	N/R	N/R	TAH + BSO	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Fujii et al. [22]	69	F	N/R	23	TAH + BSO	N/R	No	No	36	No	36	NED
Nelson et al. [12]	35	F	Abdominal pain	20	TAH + BSO + PLND	N/R	No	No	22	N/A	22	NED
Senda et al. [21]	42	F	N/R	11	Mass excision only	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Chida et al. [23]	42	F	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Seki et al. [24]	42	F	Asymptomatic	11	N/R	Intact	No	N/R	N/R	N/A	N/R	N/R
Roberto et al. [21]	45	F	N/R	20	TAH + BSO + omentectomy + PLND	N/R	N/R	No	16	N/A	16	NED
Sondengaard et al. [25]	37	F	N/R	13	Mass excision only	N/R	No	No	18	N/A	18	NED
Horiuchi et al. [21]	55	F	N/R	18	Mass excision only	N/R	YES	No	19	N/A	19	NED
Jorgersen et al. [26]	38	F	Asymptomatic	8	Mass excision only	N/R	No	No	9	N/A	9	NED
Park et al. [27]	40	F	Abdominal mass	24	TAH + BSO + omental biopsy	N/R	No	No	3	N/A	3	NED
Saikawa et al. [21]	50	F	N/R	17	Mass excision only	N/R	N/R	No	4	N/A	4	NED
Gotoh et al. [28]	44	F	Asymptomatic	12.5	N/R	Intact	Yes	Yes	2	N/R	4	DOD
Motoyama et al. [29]	42	F	N/R	11	Mass excision only	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Tenti et al. [30]	46	F	Abdominal mass	20	TAH + BSO	Ruptured	YES	No	33	N/A	33	NED
Tenti et al. [30]	45	F	Abdominal mass	20	TAH + BSO + omentectomy + PLND	Intact	No	Yes	2	N/R	19	AWD
Carabias et al. [31]	43	F	Abdominal mass	15	TAH + BSO + appendicectomy + cholecystectomy	N/R	No	No	24	N/A	24	NED
Dore et al. [32]	45	F	N/R	20	Mass excision only	N/R	No	No	16	N/A	16	NED
Lee et al. [33]	45	F	Abdominal distension	17	TAH + BSO	intact	No	No	15	N/A	15	NED

Table 1 continued

References	Age (years)	Gender	Presenting symptom	Size, max. diameter (cm)	Surgical treatment in addition to tumour resection	Mass removal	Chemo therapy	Recurrence	DFS	Recurrence site	OS	Status
Lee et al., 1996 [33]	55	F	Abdominal distension	20	TAH + BSO + omentectomy + PLND + PALND	Intact	No	No	30	N/A	30	NED
Uematsu et al., 2000 [34]	86	F	Abdominal mass	23	Gastrectomy	Ruptured	No	No	72	N/A	72	NED
Shin et al. [35]	44	F	N/R	N/R	N/R	N/R	No	N/R	N/R	N/A	N/R	N/R
Suzuki et al. [36]	40	F	Abdominal distension	15	Appendicectomy + cecum colectomy	N/R	No	No	15	N/A	15	NED
Matuno et al. [21]	39	F	N/R	20	Mass excision only	N/R	N/R	No	24	N/A	24	NED
Kaku et al., 2001 [21]	38	F	N/R	16	Mass excision only	N/R	Yes	Yes	18	N/R	18	DOD
Kessler et al. [37]	38	F	N/R	11	Descending colon resection + appendicectomy	N/R	N/R	No	60	N/A	60	NED
Tangjitgamol et al. [2]	41	F	Abdominal mass	12	TAH + BSO + omentectomy + PLND + PALND + appendicectomy	Intact	Yes	No	18	N/A	18	NED
Kawai et al. [21]	20	F	N/R	7	Mass excision only	N/R	N/R	No	18	N/A	18	NED
Mikami et al. [38]	38	F	Abdominal distension	16	TAH + BSO + omentectomy + PLND + PALND + appendicectomy	N/R	YES	Yes	18	Peritoneum	18	DOD
Song et al. [39]	72	F	N/R	12	Mass excision only	N/R	No	Yes	2	N/R	4	DOD
Sonntag et al. [40]	30	F	N/R	5	Mass excision only	N/R	No	No	12	N/A	12	NED
Izumi et al. [41]	41	F	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Kuroda et al. [21]	33	F	N/R	15	Mass excision only	N/R	N/R	Yes	N/R	N/R	N/R	DOD
Law et al. [42]	35	F	Abdominal pain	11	Mass excision only	N/R	No	No	60	N/A	60	NED
Junuzovic et al. [43]	43	F	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Fan et al. [44]	68	F	N/R	17	TAH + BSO	N/R	No	N/R	N/R	N/A	N/R	N/R
Toyoda et al. [21]	72	F	N/R	5.5	Mass excision only	N/R	N/R	Yes	3	N/R	3	DOD
De Leon et al. [9]	21	F	Abdominal pain	26	N/R	Intact	No	Yes	6	N/R	6	AWD
De Leon et al. [9]	36	F	Abdominal distension	19	Omentectomy + sigmoid resection	N/R	Yes	Yes	8	Peritoneum	9	AWD
Lee et al. [45]	32	F	Abdominal mass	15	N/R	intact	YES	No	42	N/A	42	NED

Table 1 continued

References	Age (years)	Gender	Presenting symptom	Size, max. diameter (cm)	Surgical treatment in addition to tumour resection	Mass removal	Chemo therapy	Recurrence	DFS	Recurrence site	OS	Status
Moral et al. [46]	47	F	N/R	24	N/R	N/R	No	No	8	N/A	8	NED
Tjalma et al. [47]	74	F	Abdominal pain	3	N/R	N/R	Yes	Yes	8	PELVIS	31	DOD
Kashima et al. [48]	28	F	Abdominal pain	17	N/R	intact	No	Yes	13	N/R	13	AWD
Tando et al. [21]	42	F	N/R	12	Mass excision only	N/R	N/R	No	2	N/A	2	NED
Horie et al. [49]	31	F	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Ichiya et al. [50]	56	F	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Roma et al. [51]	35	F	Abdominal pain	13	Mass excision only	N/R	No	No	13	N/A	13	NED
Roma et al. [51]	47	F	Abdominal mass	21	N/R	N/R	No	No	1	N/A	1	NED
Roma et al. [51]	24	F	Abdominal mass	18	N/R	N/R	No	No	2	N/A	2	NED
Roma et al. [51]	43	F	Abdominal mass	10	N/R	N/R	No	Yes	5	N/R	5	DOD
Roma et al. [51]	40	F	Abdominal mass	11	N/R	N/R	No	Yes	9	N/R	9	DOD
Roma et al. [51]	27	F	Abdominal mass	8	N/R	N/R	No	No	11	N/A	11	NED
Roma et al. [51]	63	F	Abdominal mass	7.5	N/R	N/R	No	Yes	14	N/R	14	AWD
Roma et al. [51]	31	F	Abdominal mass	18	N/R	N/R	No	Yes	26	N/R	26	AWD
Roma et al. [51]	48	F	Abdominal mass	26	N/R	N/R	No	Yes	58	N/R	58	AWD
Roma et al. [51]	40	F	Abdominal mass	15	N/R	N/R	No	No	58	N/A	58	NED
Roma et al. [51]	35	F	N/R	N/R	N/R	N/R	No	No	91	N/A	91	NED
Roma et al. [51]	49	F	Abdominal mass	11	N/R	N/R	No	No	130	N/A	130	NED
Roma et al. [51]	20	F	N/R	N/R	N/R	N/R	No	N/R	N/R	N/A	N/R	N/R
Dierickx et al. [52]	50	F	Abdominal distention	13	TAH + BSO + omentectomy + PLND + appendicectomy	N/R	Yes	No	58	N/A	58	NED

Table 1 continued

References	Age (years)	Gender	Presenting symptom	Size, max. diameter (cm)	Surgical treatment in addition to tumour resection	Mass removal	Chemo therapy	Recurrence	DFS	Recurrence site	OS	Status
Jiang et al. [10]	21	F	Back pain	14.6	N/R	Ruptured	Yes	Yes	4	Peritoneum	6	AWD
Kanayama et al. [1]	40	F	Abdominal distention	25	RSO + PLND + PAND	Intact	No	Yes	6	N/R	6	AWD
Cupp et al. [48]	39	F	Abdominal pain	20	N/R	N/R	Yes	N/R	N/R	N/A	N/R	N/R
Dong et al. [9]	52	F	Asymptomatic	3.8	Laparoscopy	N/R	No	N/R	N/R	N/A	N/R	N/R
Kurita et al. [16]	30	F	Abdominal pain	19	Mass excision only	Intact	No	Yes	24	Ovary	32	AWD
Hanhan et al. [54]	37	F	Abdominal mass	22	Mass excision only	Intact	No	N/R	N/R	N/A	N/R	N/R
Rivera et al. [55]	N/R	F	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Dastranj T et al. [56]	32	F	abdominal	10.5	Omentectomy	Omental spread	N/A	N/A	N/A	N/A	1	DOD
Myriokefalitaki et al current case	56	F	Abdominal pain	24	TAH + BSO + omentectomy + appendicectomy	N/R	No	No	17	No	17	NED
Kamiyama et al. [57]	62	F	Abdominal pain	10	N/R	Multiple cysts	No	Yes	8	Bone	15	DOD
Green et al. [58]	83	M	Abdominal pain	26	N/R		No	No	6	N/A	6	NED
Thamboo et al. [59]	64	M	Abdominal distention	24	N/R	.	No	No	18	N/A	18	NED
Hrora et al. [7]	42	M	Abdominal pain	5	N/R	Multiple masses	No	No	6	N/A	6	NED
Shiau et al. [60]	59	M	Back pain	7.5	N/R	Intact	No	No	79	N/A	79	NED
Feng et al. [16]	63	M	Back pain	4	N/R		No	N/R	13	N/A	13	NED

F female, *M* male, *N/R* not recorded/not reported, *TAH* total abdominal hysterectomy, *BSO* bilateral salpingo-oophorectomy, *PLND* pelvic lymph node dissection, *PAND* para-aortic lymph node dissection, *RSO* right salpingo-oophorectomy, *DOD* dead of disease, *NED* no evidence of disease, *AWD* alive with disease

Table 2 Chemotherapy regime following Primary Retroperitoneal Mucinous Cystadenocarcinoma, $n = 13$

Author (year)	Age (years)	Size, max. diameter (cm)	Surgical treatment additional to tumour resection	Mass removal	Adjuvant chemotherapy	Cycles	Recurrence	Recurrence (months) post surgery	Follow-up (months)	Death
Douglas et al. [19]	18	5	N/R	N/R	N/R	N/R	Yes	Yes	N/R	DOD
Horiuchi et al. [21]	55	18	N/R	N/R	Cyclophosphamide + adriamycin/doxorubicin + cisplatin	N/R	No	N/R	19	NED
Gotoh et al. [28]	44	12.5	N/R	Intact	Cisplatin + mitomycin	N/R	Yes	2	4	DOD
Tenti et al. [30]	46	20	TAH + BSO	Ruptured	Cisplatin	5	No	No	33	NED
Kaku et al., 2001 [21]	38	16	N/R	N/R	Cyclophosphamide + adriamycin/doxorubicin + cisplatin + paclitaxel	N/R	Yes	N/R	18	DOD
Tangjitgamol et al. [2]	41	12	TAH + BSO + appendicectomy + omentectomy + PLND + PALND	Intact	Cyclophosphamide + cisplatin	6	No	No	18	NED
Mikami et al. [38]	38	16	TAH + BSO + appendicectomy + omentectomy + PLND + PALND	N/R	Cyclophosphamide + adriamycin/ doxorubicin + cisplatin	N/R	Yes	Yes	18	DOD
De Leon et al. [9]	36	19	Omentectomy + sigmoid resection	N/R	Carboplatin + paclitaxel	N/R	Yes	8	9	AWD
Lee et al. [45]	32	15	N/R	Intact	Cyclophosphamide	N/R	No	No	42	NED
Tjalma et al. [47]	74	3	N/R	N/R	Carboplatin	4	Yes	8	31	DOD
Dierickx et al. [52]	50	13	TAH + BSO + appendicostomy + omentectomy + plnd	N/R	Carboplatin	6	N/R	N/R	58	NED
Jiang et al. [10]	21	14.6	N/R	Ruptured	Oxaliplatin + 5-fluorouracil	N/R	Yes	4	6	AWD
Cupp et al. [53]	39	20	N/R	N/R	Carboplatin + paclitaxel	N/R	N/R	N/R	N/R	N/R

N/R not recorded/not reported, *TAH* total abdominal hysterectomy, *BSO* bilateral salpingo-oophorectomy, *PLND* pelvic lymph node dissection, *PAND* para-aortic lymph node dissection, *RSO* right salpingo-oophorectomy, *DOD* dead of disease, *NED* no evidence of disease, *AWD* alive with disease

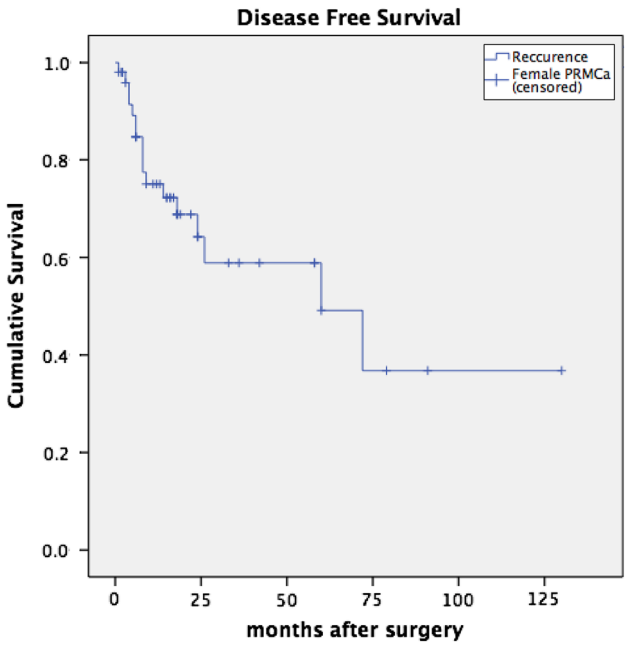

Fig. 2 Disease-free survival (female cases, $n = 73$)

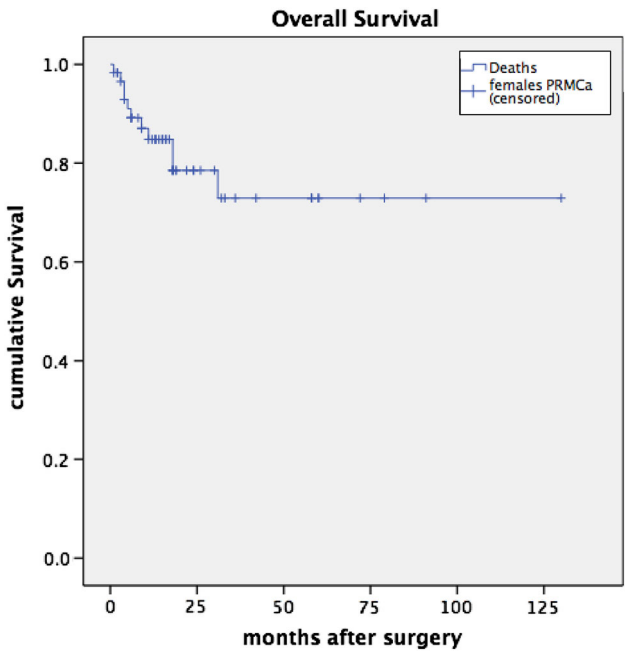

Fig. 3 Overall survival (female cases, $n = 73$)

system and pancreas or renal cystic disease, renal lymphangioma or hydatid cysts [7].

The most commonly used radiological investigations were ultrasonography (USS) and computed tomography (CT). Imaging is unable to distinguish between the different types of mucinous carcinoma [8], however, magnetic resonance imaging (MRI) is able to further characterise these lesions and identify their mucinous component. Although USS, CT and MRI clearly detect cystic masses in ovarian or pelvic organs, diagnosis of a retroperitoneal tumour is challenging and their retroperitoneal origin is often only revealed intraoperatively [9].

Tumour markers including carcinoembryonic antigen (CEA), carbohydrate antigen CA19.9, CA15.3, CA125 and alpha fetoprotein (AFP) are not specific or sensitive to aid diagnosis or guide management. Jiang et al. [10] reported a case where tumour markers stopped increasing even though the tumour continued to grow. Reviewing all the cases, the tumour marker levels at the time of diagnosis have not been shown to be of any benefit and are poor in estimating either tumour size or stage. Increased tumour marker levels can be an indication of recurrence, especially CA125 when there is peritoneal disease spread.

A staging laparotomy is essential to assess the true extent of disease and surgical treatment with complete excision of the mass is the cornerstone of treatment, with oophorectomy not adding to survival benefit. Removal of the mass intact has not been proven to be a statistical significant prognostic factor but this might be because of the small number of cases that this additional information has been reported. Tumour rupture occurred during removal in 23.3 % of the cases that had a recurrence and 33.3 % of those did not during the reported follow-up period ($p > 0.05$). Spillage of tumour cells during surgical excision is to be avoided if possible, however, it may not always be technically feasible to remove a strongly adherent or invading tumour intact.

Unfortunately, a staging classification for PRMCa does not exist; cases have been treated as per TNM (Tumour, Node, Metastasis) staging system. In most cases, lymph node assessment was not performed, and therefore, early-stage cases may have had occult distant disease at the time of diagnosis, which may account for the high recurrence rate.

Thus far the benefit of adjuvant chemotherapy in the management of mucinous adenocarcinoma is not well known. It has been considered in cases where there has been intra-operative tumour rupture, capsule involvement or identified metastatic disease [11]. In the above meta-analysis we did not identify a survival benefit with adjuvant chemotherapy, although this outcome is biased due to the fact that chemotherapy was given only to select high-risk group as described above.

With regards to tumour recurrence rate, there was no observed difference in the mean age at diagnosis (43.6 years) compared to those who did not have recurrence (41.0 years) ($p = 0.51$). Neither there was any difference in the size of tumour mass 6.8 cm (SE 1.6) versus 5.4 cm (SE 1.0), $p = 0.07$. This could be due to rupture of

tumour or lymph node involvement that was not known or reported for the cases. Nelson et al. [12] suggested that close follow-up and tailoring of management to the individual patient's condition, leads to improved outcome. Due to the retroperitoneal location of the tumour it is unlikely that disease recurrence will be detected on clinical examination and therefore cross-sectional imaging needs to be included in the follow-up schedule.

One of the major limitations of this review is the lack of RCTs or large observational studies. Although, it is difficult to judge the quality of evidence obtained from case reports, in the absence of any other study designs, these form the basis of guiding clinical management of rare conditions [13, 14]. With case reports and case series, we faced the dilemma of missing data, variation in management and short reported follow-up, which limited the analysis of pooled results to come to definite conclusions regarding risk factors or predictors for this disease. The result of this meta-analysis emphasises the need for complete staging, fertility preservation option and survival rates which would be useful in counselling women in clinical practice.

Moreover, we have noticed a shift in chemotherapeutic agents used over the years from CA and CAP to Carboplatin and Paclitaxel. Platinum-based chemotherapy has been consistently given as PRMCa has been considered to be of ovarian origin. Although, the exact origin and histopathogenesis of this tumour is not well known, there have been various theories including retroperitoneal location of an ectopic ovary [15], although there are male cases reported [16], origin from retroperitoneal primary monodermal teratoma, enterogenous genesis from intestinal duplication and more recently considered to originate from invagination of peritoneal mesothelial cells [17]. In view of this, it stays debatable as to which chemotherapeutic regime would be the best treatment option and whether all patients should be considered for adjuvant chemotherapy, more so because staging of PRMCa is not established.

To our knowledge, this is the first meta-analysis of PRMCAs and attempt to extract conclusions and guidance for clinical management and consultation for these patients. There are limitations in performing meta-analysis on case reports; however, combining what data is available in the published literature in order to evaluate disease progression and management of rare cases means that trends and themes can be identified. This study highlights the need for having an established reporting proforma for rare diseases so that a minimum standard of clinical and management information can be obtained and help provide meaningful results with meta-analyses. We agree that the implementation of the CARE (Case REport) guidelines by medical journals will improve the extraction of conclusions [18].

Conclusion

The rarity of PRMCa poses challenges in terms of appropriate management; however, by reviewing of these cases a more consistent approach to managing the patient can be set. Fertility-sparing surgery is an acceptable option since oophorectomy has not been shown to have an influence on prognosis. Appropriate surgical staging and identification of risk factors should be sought in order to select case that will benefit of adjuvant chemotherapy. Based on this systematic review and meta-analysis of PRMCa cases, we would advise regular follow-up with imaging during the first 2 years following diagnosis since recurrences typically occur within this time frame.

Compliance with ethical standards

Conflict of interest No conflict of interest.

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