REVIEW

Epidemiology of cancer in older adults: a systematic review of age-related differences in solid malignancies treatment

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Abstract

Purpose of review We examined the latest epidemiological research on age-related differences in cancer treatment and selected outcomes, among patients with cancer aged 60 and above in comparison to younger patients.

Recent findings Colorectal, pancreatic and lung cancers were studied most often. Most studies were conducted in Europe or the United States of America (USA) within single centers. For unselected patients, older patients receive less treatment, and their survival, regardless of the metric used (cancer-specific survival or overall survival), was poorer than that of middle-aged patients. Age-related differences in treatment and outcomes were more pronounced in patients aged over 80 years. However, among patients selected for treatment, complications, adverse events rates and survival probabilities were comparable between older and younger patients. Treatment differences, especially the omission of therapy, were often smaller for good prognosis cancer types.

Summary The likelihood of receiving treatment decreased as age increases, regardless of the cancer types, treatment, countries and setting. More research on treatment in older patients with cancer, especially the frailest and the oldest, is urgently needed as there is still a lack of data to tailor treatment.

Keywords Epidemiology · Aging · Therapy · Outcomes

Introduction

Due to the ageing of the global population, cancer burden in older adults is increasing. Worldwide, the number of people aged 65 years or older is projected to more than double [1], with an even faster growth in people over the age of 80 years [2, 3]. Most older people are fit, however, others might be frail or chronically ill as a result of the physiological changes in organ systems, more prevalent diseases, and other changes associated with ageing [4]. As adults age in different ways and with different trajectories, the older population is very heterogeneous in terms of health and functional status [5]. The presence of comorbidities, poorer health status and advanced cancer stage at diagnosis, as well as patient preferences, are usually mentioned to deviate from guideline adherent treatment for selected older patients.

Epidemiological observational studies play a crucial role in the (post market approval) evaluation of treatment and outcomes as they provide real-world evidence for all patients, identify complications and adverse events and study long-term safety [6]. In particular, observational studies can be useful studying large heterogeneous patient populations and highlight disparities across age groups, thereby guiding research and interventions. Over the past years, literature on cancer treatment in older patients has grown; there are, however, conflicting results on the treatment differences between younger or middle-aged and older patients, differences with respect to changes in treatment over time, and not all tumor types have been described. In addition, the settings (single center reports or larger population-based studies), countries and age cut-off are mostly scattered. As the number of publications in the geriatric oncology field has increased in recent years, it is crucial to provide an overview of the recent literature on treatment in older adults. Therefore, this systematic review aims to synthesize the latest research on

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the age-related differences in cancer treatment, and selected outcomes, among patients with cancer aged 60 and above in comparison to younger patients.

Methods

Search Strategy and Article Selection

The literature review protocol was pre-registered in PROS-PERO (CRD42023450654); results are described in two papers, one focusing on prevalence, incidence, and mortality in general and more specifically on age-related survival differences and associated factors [7]; and the present one focusing on age-related differences in treatment strategies and associated outcomes. We searched papers published from January 1st, 2019 until August 3, 2023 in Embase and MEDLINE. The search strategy was first set up in MED-LINE and then adapted for Embase using search terms corresponding to "older adults", "cancer", and "therapy". Older adults were defined as 60 years or older following the definition of the United Nations.

Figure 1 shows the selection of articles. Duplicate records were removed before the screening. Two independent reviewers screened titles and abstracts with the following inclusion criteria for the present review: 1) the paper was primarily focused on treatment differences; 2) between young and older patients (60 years or older, any cut-off was acceptable) with cancer; and 3) published in English. Exclusion criteria were: 1) no age group comparison in the paper or only two extreme age groups compared (e.g. 80 + versus 40 and younger), 2) focus only on survival outcomes, 3) inclusion of a small subset of patients with a specific stage (e.g. stage Ia) or studies that assessed a new surgical technique or a new or very selected (non-standard) systemic treatment. Conference abstracts, reviews of any kind, editorials, or letters to editors were also excluded. There was no restriction on the study outcomes and geography. Any disagreements were resolved by referral to a third reviewer. Next, the full text of all remaining papers was obtained.

Data Extraction

First, general study characteristics as first author, year of publication, cancer site, country, study years, setting and the number of patients in the study were extracted from the articles. With respect to the setting, population-based studies had to include all consecutive patients from a registry, single center from a single hospital or cancer center. Studies were sorted on the cancer localization. Next, the following data with respect to studies reporting treatment differences in general were extracted: age categories as used in the article, treatment percentages for the younger and older age groups

and in some papers for a middle age group or an old age group defined as 80 years or older, p-values for the difference and a summary of the differences in outcomes. Studies were sorted by the age cut-off and cancer type (based on low or high survival). Finally, the following data was extracted from studies that described age-related differences in populations receiving a specific treatment: cancer site, age cut-off, treatment and outcomes, percentages in the age groups and p-value; for articles that described surgical treatment we extracted 30-day (or 90-day) mortality, complications or adverse events (when combined with systemic treatment), and survival or recurrence data. When an article reported several specified adverse events, only the combined percentages or the most frequent adverse event was extracted. For studies reporting about age-related differences in systemic treatment, we additionally extracted data with respect to adverse events or toxicity, information on the dose or number of cycles, and time to progression where applicable. Zotero V.6.0.36 was used to manage references and Rayyan [8] for the title, abstract and full-text screening.

Results

Overall, we selected 440 papers for full-text review and excluded 339 papers, subsequently, 101 papers were included, and 1 study that fulfilled the inclusion criteria, however not present in the full-text review selection, was added by SP [7], resulting in the inclusion of 102 articles. Table 1 describes the characteristics of the included studies, sorted by tumor type. Fifteen studies focused on tumors specifically in females, namely breast [9–12], cervical [13–16], ovarian [17–20], endometrial [21, 22] or vulvar [23] cancers. A large proportion of the studies assessed age-related differences in treatment for rectal (n = 10) [24–33], colon (n = 6) [34–39], or colorectal cancers (n = 7) [40–46]. Gastric cancer was studied in 5 studies [47–51] and esophageal cancer in 7 studies [52–58]. A large number of studies focused on pancreatic cancer (n = 12) [59–70], and lung cancer (n = 9) [71–79] including Small Cell Lung Cancer (SCLC) [78] and Non-Small Cell Lung Cancer (NSCLC) [74–77, 79]. Seven studies assessed age-related differences in treatment and outcomes in the metastatic setting [80–86]. The largest number of studies used data from Europe (36%), 24 studies from the USA (23%), and 15 from Japan (15%). Most studies were from large single centers (56%), 29 were population-based (28%), and the remaining were multicenter studies.

Age-Related Treatment Differences for Unselected Patients (Table 2, part A)

Regardless of the age cut-off used and the treatment studied, older adults are more likely to receive no treatment or
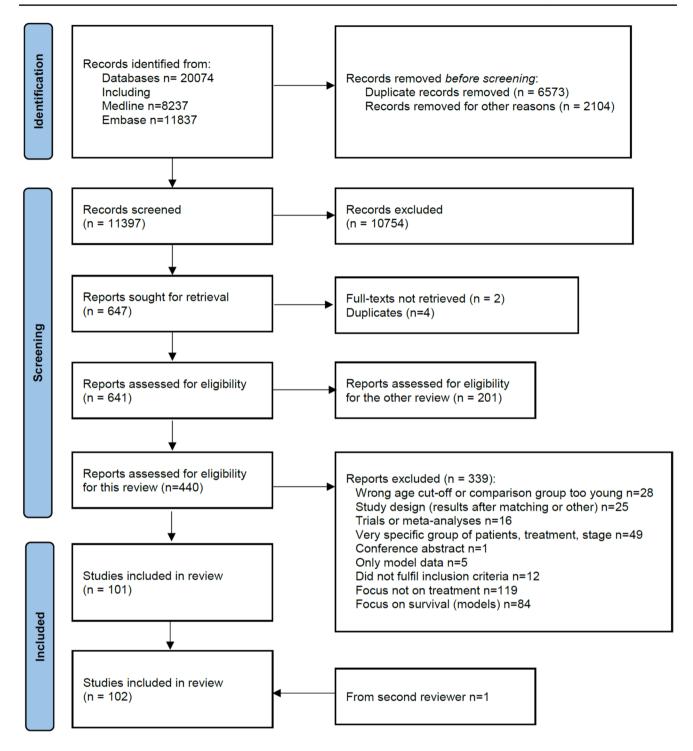
Fig. 1 Flow diagram of the review

no (neo)adjuvant treatment, and have poorer survival than younger adults. Remarkably, in a study, palliative treatment was administrated in a higher percentage to older patients with anal cancer (16.1%) than younger patients (11.2%) [87], as well as bypass or stoma for rectal cancer; 5%, 10% and 26% for < 65, 65–79 and 80 + years

respectively [31]. One study on cervical cancer did not show differences in chemotherapy rates across age categories; 47.3% for under 65 years versus 47.0% for patients of 65 years and older [14]. For the studies that used 80 years as a cut-off [56, 63, 88], age-related differences in

Table 1 Characteristics of the included studies on age-related differences in treatment by cancer site

First author, year	Cancer site	Country	Study year*	Setting**	Nr patients[#]
Tan, 2021[12]	Breast	Malaysia	2010–2014	Population-based	2166
Drapalik, 2022[9]	Breast	USA	2005–2017	Population-based	172272
Jauhari, 2019[10]	Breast	UK	2014–2016	Population-based	12716
Buonomo, 2023[11]	Breast	Italy	2016–2022	Single center	231
Hou, 2020[13]	Cervical	Taiwan	2007–2016	Single center	123
Xie, 2020[14]	Cervical	USA	2004–2015	Population-based	36816
Barben, 2022[15]	Cervical	France	2005–2015	Population-based	292
Neumeyer, 2023[16]	Cervical	Germany	2004–2013	Population-based	14528
Joueidi, 2020[17]	Ovarian	France	2000–2016	Multicenter	979
Pinelli, 2021[18]	Ovarian	UK	2016–2018	Single center	114
Zambrano-Vera, 2021[19]	Ovarian	USA	1999–2018	Single center	148
Van Walree, 2019[20]	Ovarian	Netherlands	2010–2015	Single center	128
Hotton, 2020[21]	Endometrium	France	2007–2016	Single center	148
Luzarraga-Aznar, 2022[22]	Endometrium	Spain	2010–2019	Single center	281
Hellman, 2020[23]	Vulva	Sweden	2012–2016	Population-based	657
Peltrini, 2021[24]	Rectal	Italy	2011–2020	Multicenter	287
Sonal, 2023[25]	Rectal	USA	2004–2018	Population-based	328
Mourad, 2021[26]	Rectal	Australia	2006–2018	Single center	699
Inanc, 2022[27]	Rectal	Turkey	2011–2018	Single center	175
De Nes, 2022[28]	Rectal	Netherlands	2008–2016	Population-based	6524
Birch, 2019[29]	Rectal	UK	2009–2014	Population-based	52922
Kang, 2021[30]	Rectal	Australia	2006–2015	Multicenter	736
Høydahl, 2022[31]	Rectal	Norway	1980–2016	Single center	666
Liu, 2020[32]	Rectal	China	2010–2018	Single center	414
Chesney, 2020[33]	Sigmoid & rectal	Canada	2002–2018	Single center	792
Hayes, 2019[34]	Colon	UK	1999–2010	Population-based	31910
Liu, 2023[35]	Colon	China	2004–2017	Single center	416
Mazzola, 2023[36]	Colon	Italy	2015–2018	Single center	130
Oytun, 2022[37]	Colon	Turkey	2010–2015	Single center	465
Shafiei, 2020[38]	Colon	Australia	2000–2010	Single center	1135
Hagerty, 2022[39]	Colon	USA	2010–2016	Single center + registry	14966
Ogata, 2022[40]	Colorectal	Japan	2013–2017	Single center	346
Cheng, 2022[41]	Colorectal	China	2011–2020	Single center	2084
Shiraishi, 2023[42]	Colorectal	Japan	2013–2021	Single center	215
Kryzauskas, 2021[43]	Colorectal	Lithuania	2014–2018	Single center	900
Cross, 2021[44]	Colorectal	Australia	2007–2018	Multicenter	20463
Okamoto, 2022[45]	Colorectal	Japan	2010–2021	Single center	138
Sarasqueta, 2019[46]	Colorectal	Spain	2010–2012	Single center	1157
Miller, 2022[87]	Anus	USA	2004–2015	Population-based	26796
Lee, 2022[105]	Gastrointestinal	Korea	2018–2020	Single center	477
Xu, 2021[47]	Gastric	China	2009–2014	Single center	306
Otowa, 2019[48]	Gastric	Japan	2014–2017	Single center	195
Keywani, 2023[49]	Gastric	Netherlands	2015–2019	Population-based	1995
Komori, 2020[50]	Gastric	Japan	2000–2012	Single center	411
Esaki, 2019[51]	Gastric	Japan	2000–2011	Multicenter	1969
Laurent, 2022[52]	Esophageal	Belgium	2006–2015	Single center	248
Kanda, 2019[53]	Esophageal	Japan	2005–2017	Single center	150
Cooper, 2021[54]	Esophageal	USA	2016–2020	Single center	201
Suzuki, 2022[55]	Esophageal	Japan	2010–2020	Single center	174
Bakhos, 2019[56]	Esophageal	USA	2004–2014	Population-based	107921

Table 1 (continued)

First author, year	Cancer site	Country	Study year*	Setting**	Nr patients[#]
Baranov, 2022[57]	Esophageal	Netherlands	2011–2019	Audit	3775
Klevebro, 2019[58]	Esophageal, Gastric	Sweden	2007–2017	Single center	548
Vithayathil, 2022[92]	Hepatocellular	International	2020–2021	Single center	191
Marta, 2021[106]	Hepatocellular	Brazil	2007–2017	Single center	238
Shimada, 2020[107]	Hepatocellular	Japan	2000–2017	Single center	796
Inoue, 2019[108]	Hepatocellular	Japan	2001–2016	Single center	530
Liu, 2021[109]	Liver	Australia	2001–2017	Single center	357
Van Dongen, 2022[59]	Pancreas	Netherlands	2015–2018	Population-based	10298
Ramanathan, 2019[60]	Pancreas	USA	2014–2015	Population-based	1626
Gruppo, 2020[61]	Pancreas	Italy	2012–2017	Single center	124
Hackner, 2022[62]	Pancreas	Germany	2000–2018	Single center	213
Li, 2020[63]	Pancreas	USA	2004–2015	Population-based	140678
Elias, 2022[64]	Pancreas	USA	2015–2020	Population-based	5973
Henry, 2022[65]	Pancreas	Netherlands	2014–2016	Multicenter	836
Brada, 2021[66]	Pancreas	Netherlands	2015–2017	Multicenter	422
Sawyer, 2021[67]	Pancreas	USA	2011–2019	Single center	225
Izumo, 2021[68]	Pancreas	Japan	2000–2018	Single center	579
Oba, 2021[69]	Pancreas	USA	2011–2019	Single center	246
Malik, 2020[70]	Pancreas	UK	2005–2014	Single center	222
Sahli, 2021[110]	Thyroid	USA	2004–2015	Population-based	1457
Matrone, 2020[111]	Thyroid	Italy	2000–2018	Single center	432
Walter, 2019[71]	Lung	Germany	2009	Population-based	17478
Pham, 2021[72]	Lung	Australia	2011–2017	Population-based	3481
De León, 2021[73]	Lung	USA	2016–2019	Single center	673
Cao,2019[112]	LCNEC	USA / China	2004–2013	Population-based	1619
Grosjean, 2021[74]	NSCLC	Canada	2010–2019	Single center	327
Galli, 2019[79]	NSCLC	Italy	2013–2019	Single center	290
Zaborowska-Szmit, 2021[75]	NSCLC	Poland	2010–2014	Single center	196
Okishio, 2020[76]	NSCLC	Japan	2016–2016	Multicenter	901
Pilleron, 2023[77]	NSCLC	UK	2014–2017	Population-based	20716
Takeda, 2023[78]	SCLC	Japan	2019–2022	Single center	155
Linton, 2019[113]	MPM	Australia	2002–2009	Registry	1121
Pan, 2022[114]	MPM	USA	1975–2016	Population-based	1492
Lemiński, 2022[89]	Bladder	Poland	2003–2021	Single center	568
Sirithanaphol, 2019[115]	RCC	Thailand	2007–2017	Single center	101
Nemoto, 2022[91]	RCC	Japan	2013–2020	Multicenter	149
Bryant, 2022[116]	Prostate	USA	2000–2015	Population-based	12784
Thakur, 2020[117]	Meningioma	USA	2008–2019	Single center	291
Perla, 2021[118]	Infratentorial	USA	2012–2018	Population-based	2212
Gingrich, 2019[119]	STS	USA	2004–2012	Population-based	33859
Guertin, 2023[88]	STS	USA	2000–2015	Population-based	24666
Kotchetkov, 2023[93]	Lymphoma	Canada	2013–2022	Single center	201
Johns, 2021[120]	Mixed	USA	2011–2018	Population-based	673
Nia, 2020[121]	Mixed	USA	2008–2016	Multicenter	30,183
Storm, 2022[122]	Mixed	Netherlands	2016–2019	Single center	217
Metastatic setting					
Prager, 2021[80]	Pancreas	Austria	2015–2019	Multicenter	317
Koga, 2022[81]	Pancreas	Japan	2013–2017	Multicenter	153
Niedersüß-Beke, 2021[82]	Colorectal	Austria	2005–2020	Single center	1105
Potthoff, 2020[83]	Breast	Germany	2012–2015	Multicenter	407

Table 1 (continued)

First author, year	Cancer site	Country	Study year*	Setting**	Nr patients#
Araujo, 2021[84]	RCC	International	2009–2019	Multicenter	1427
Lemelin, 2020[85]	Neuroendocrine	France	1990–2017	Single center	866
Liao, 2022[86]	Gastric	Taiwan	2009–2019	Single center	428

*Only study year extracted, irrespective of the months, **Population-based: consecutive patients from a registry, single center from a single hospital or cancer center, #studies including a relatively small number (< 100 patients in total) of patients were excluded, MPM = Malignant pleural mesothelioma, LCNEC = large cell neuroendocrine carcinoma, RCC = Renal cell carcinoma, STS = Soft tissue sarcoma

treatment were more pronounced, especially in the non-receipt of chemotherapy, with difference going up to 34% [63].

Differences in treatment rates, especially assessing the non-receipt of therapy, were often less than 10% between younger and older patients aged over 60 or 65 diagnosed with a good prognosis cancer, such as breast cancer [12]. An exception to this is one study in patients with cervical cancer, where 62% of the younger patients underwent surgery, compared to 36% in the older group [14]. For patients diagnosed with poor-prognosis cancers such as lung or pancreatic cancer, differences in treatment rates across age groups were most often larger. For instance, in patients with pancreatic cancer, 33% of the younger patients received no treatment versus 67% of the patients over 60 years [59]. For lung cancer, age-related differences were smaller, although a study reported larger differences with 4.4% of the younger patients who did not received treatment versus 20.2% in those over 65, and 54.7% in those over the age of 80 years [71].

Age-Related Treatment and Outcome Differences for Selected Patients (Table 2, part B)

For patients who underwent surgery, older patients were consistently less likely to receive neo-adjuvant or adjuvant therapy regardless of the cancer type [17, 18, 22, 36, 38, 44, 46, 48, 52, 53, 55, 57, 58, 62, 65, 68, 70, 89].For those receiving systemic treatment, the completion rate was lower in older patients [53, 54, 76]. Overall mortality, 30-day mortality, long-term survival and disease-free survival were worse in older patients in most of the studies. Age-related differences in treatment and outcomes were more pronounced from the age of 80 years, for example in colorectal cancer where more complications and a higher 30-day mortality were recorded: 13% versus 21% for colon cancer and 11% versus 23% for rectal cancer and a 30-day mortality of 0.9 versus 3.3 for colon and 0.4 versus 3.1 for rectal cancer, respectively [44]. Older patients were less likely to receive adjuvant chemotherapy; however, once selected for treatment, their complications and adverse events rates were similar to younger patients [39, 42, 45]. With respect to patients receiving immunotherapy, the number of cycles or median doses received was similar between younger and older patients [76, 90]. Among patients receiving immunotherapy or chemotherapy, overall and progression free survival was comparable across age groups in most of the studies [74, 76, 79–81, 90–93].

Assessing those poor prognosis cancer types, for example pancreatic cancer, complications after surgery are usually not significantly different across age groups [61, 62, 65]. For colon or colorectal cancer, postoperative complications were significantly different between the age groups in some studies [41, 44], while other showed similar rates [36] which might be explained by differences in patients characteristics selected for surgery or not.

Discussion

The present systematic review describes the recent literature on differences in treatment and outcomes between younger and older patients with cancer. Most articles reported studies on colorectal, pancreatic and lung cancers, and were usually from single centers in Europe or the USA. For unselected patients, older patients still receive less (systemic) treatment and more often no treatment. Besides, survival, regardless the metric used, was poorer in older patients, with more pronounced differences in patients over the age of 80 years. However, for selected patients, especially for surgery, immunotherapy or chemotherapy, complications or adverse events as well as survival were usually comparable between older and younger patients. It is urgent to improve the representation of older adults in cancer treatment research to help narrow down age-related disparities in treatment receipt and outcomes.

It is tempting to speculate why older patients are less likely to receive treatment, and whether this is undertreatment or tailored treatment. Many valid reasons can explain why patients do not receive treatment: patients' health status and frailty, restricted risk–benefit balance, limited life expectancy, or patients' preference [71]. However, the lack of scientific evidence on the effectiveness of treatment, specifically in multimorbid and oldest patients [82] can

Table 2 Part A: Age-related differences in treatment for unselected patients, by age cut-off and tumour type sorted by population 5-year survival (high > 50% and low ≤ 50% (International Agency for Research on Cancer, World Health Organization)). Part B: Age-related differences in treatment and outcomes for specific treatment-selected patients

A. Age-related differences in treatment for unselected patients, by age cut-off and tumour type sorted by 5-year survival (high > 50% and low ≤ 50%)

Author, year	Cancer site	Age	Treatment	Young (%)	Middle (%)	Older 60+, 65+, 70+, 75+ (%)	Old 80+ (%)	p-value	Outcome
Cut-off 60 years									
Tan, 2021[12]	Breast (high)	<40, 40–59, ≥60	No treatment Surgery only Surgery + oncologic Oncologic therapy	25.7 33.0 23.9 17.4	24.6 34.1 27.7 13.6	26.7 39.9 21.1 12.4			CSS and OS worse
Hellman, 2020[23]	Vulvar (high)	20–59, 60–69, 70–79, ≥80	Surgery Definitive RT No treatment	86 11 1	91 8 <1	76 19 5	76 12 11	0.014 0.80 <0.001	5-year OS and RS worse
Hayes, 2019[34]	Colon (high)	<60,60–69,70–79,≥80	Surgery CT surgical pts CT non-surgical pts	84.1 59.1 62.2	84.0 46.1 42.3	79.4 26.8 22.8	61.1 4.8 3.4	<0.001 <0.001 <0.001	
Van Dongen, 2022[59]	Pancreas (low)	<60, ≥60	Resection Neoadjuvant CRT Adj. chemotherapy Palliative CRT No treatment	22 18 71 43 33		14 11 53 18 67			Median OS worse
Pham, 2021[72]	Lung (low)	<60,60–69,70–79,≥80	Radiotherapy Surgery Chemotherapy Immunotherapy Any treatment	54.7 26.0 71.9 20.0 93.2	47.7 25.8 61.6 14.4 89.0	48.9 24.7 52.6 10.5 86.6	47.8 14.9 26.5 9.5 71.8	<0.001	Median survival lower
Cut-off 65 years									
Sahlia, 2021[110]	Thyroid (high)	18–64, 65–79, ≥80	No surgery Lobectomy Total thyroidectomy	3.9 5.5 90.7		4.9 7.3 87.8	11.5 10.3 78.2	0.006	CSM worse
Xie, 2020[14]	Cervical (high)	<65, ≥65	Surgery Radiotherapy Chemotherapy	62.30 52.93 47.25		36.52 65.30 47.02		<0.001 <0.001 0.741	
Neumeyer, 2023[16]	Cervical (high)	<65, ≥65	Any treatment Surgery (stages) Chemotherapy Radiotherapy	44 18–46 8–35 12–45		40 15–46 5–14 18–43			5-year RS worse
Miller, 2022[87]	Anal (high)	<65, ≥65	Concurrent CRT Local therapy Palliative therapy No treatment	65.0 21.4 11.2 2.4		54.5 25.1 16.1 4.3		<0.001	

Table 2 (continued)

Study	Cancer	Age groups	Treatment	Group 1	Group 2	Group 3	Group 4	p-value	Outcome
Mourad, 2021[26]	Rectal (high)	≤65, 66–79, ≥80	No surgery / No treatment (non-surg pts)	10 / 23	16 / 33	29 / 47		<0.001 / 0.005	Death <90d higher, OS & RS worse
Hoydahl, 2022[31]	Rectal (high)	<65, 65–79, ≥80	Resection curative / Res. noncurative / Bypass or stoma	66 / 12 / 5	72 / 8 / 10	47 / 5 / 26		<0.001	
Cao, 2019[112]	LCNEC (low)	<65, ≥65	No Surgery / Chemotherapy / Radiotherapy	57.06 / 60.08 / 43.62	61.57 / 43.93 / 33.26			<0.001 / <0.001 / <0.001	5-yr CSS worse
Walter, 2019[71]	Lung (low)	≤65, 65–74, 75–84, ≥85	No treatment / Radiotherapy / Tumor resection	4.4 / 23.7 / 34.7	7.8 / 21.9 / 35.4	20.2 / 21.4 / 27.8	54.7 / 17.1 / 15.3	<0.0001 / 0.004 / <0.0001	
Pan, 2022[114]	MPM (low)	<65, ≥65	Surgery / Radiotherapy / Chemotherapy	47.88 / 3.75 / 59.7	33.38 / 2.26 / 44.21			<0.001 / 0.1 / <0.001	5-year CSS worse
Brada, 2021[66]	Pancreas, locally advanced (low)	<65, 65–74, ≥75	Best supp care / Folfirinox	12 / 78	18 / 63	46 / 14		<0.01	Median OS worse
Cut-off 70 years									
Jauhari, 2019[10]	Breast, DCIS (high)	<70, ≥70	Surgery / Post-BCS RT	93.7 / 58.4	80.5 / 43.1				
Drapalik, 2022[9]	Breast, TN (high)	≤40, 41–70, >70	No Chemotherapy / Neoadjuvant CT / Bilateral mastectomy / No axillary surgery / No radiation	11 / 44.1 / 37 / 12 / 50	19 / 30.1 / 17 / 12 / 42	57 / 20.5 / 4 / 21 / 55		<0.001	
Barben, 2022[15]	Cervical (high)	<70, ≥70	No treatment / Surgery / Lymphadenectomy / Radiotherapy / Chemotherapy	4.4 / 81.7 / 52.9 / 49.6 / 48.2	18.7 / 37.5 / 17.0 / 67.2 / 39.1			<0.001 / <0.001 / <0.001 / 0.012 / 0.19	5-year survival worse
Kang, 2021[30]	Rectal, localized (high)	<70, ≥70	Non-operative / St III surgery alone / Neoadjuvant stage III / Adjuvant stage III / Discussed MDT	2.0 / 4.3 / 54.3 / 79.1 / 59.5	7.4 / 25.2 / 36.8 / 47.1 / 50.2			0.0014 / <0.001 / 0.007 / <0.001 / 0.01	5-yr OS and CSS worse
De Nes, 2022[28]	Rectal, locally advanced (high)	<70, ≥70	No treatment / Resection only / Neoadj + resection / Adjuvant treatment	1.6 / 4.7 / 84.4 / 9.8	10.2 / 8.3 / 62.6 / 4.6			<0.001	30-d and 90-d higher

Table 2 (continued)

Study	Cancer type	Age cut-off	Treatment category				p-value	Note
Birch, 2019[29]	Rectal (high)	<70, 70–79, ≥80	No surgery / Major resection / No radiotherapy / Stoma creation	16.0 / 66.5 / 46.4 / 73.9	21.2 / 60.6 / 55.4 / 71.8	47.5 / 31.7 / 69.5 / 65.6		Deaths <30d higher
Linton, 2019[113]	MPM (low)	<70, 70–79, ≥80	Chemotherapy / Surgery / Adjuvant RT	62.6 / 14.4 / 8.6	35 / 1.1 / 1.1	8.1 / 0.6 / 0	<0.001 / <0.001 / <0.001	Survival in months lower
Cut-off 75 years								
Gingrinch, 2019[119]	STS Extremities (high)	18–74, ≥74	No surgery / Radiation / Chemotherapy / Palliative treatment	6.2 / 48.7 / 29.1 / 0.8	11.7 / 46.6 / 14.8 / 1.9		<0.0001 / 0.002 / <0.0001 / <0.0001	90d mortality higher
Van Walree, 2019[20]	Ovarian (low)	<75, ≥75	Discussed MDT / Chemotherapy / Supportive care only	87 / 89 / 7	64 / 52 / 38		0.002 / <0.001 / <0.001	
Cut-off 80 years								
Guertin, 2023[88]	STS (high)	<80, ≥80	Surgery / Radiotherapy / Chemotherapy	86.2 / 41.5 / 20.7	74.0 / 39.1 / 3.5		<0.001 / 0.010 / <0.001	
Bakhos, 2019[56]	Esophageal (low)	<80, 80–89	Chemotherapy / Radiation / Surgery / Multimodality	65.8 / 57.5 / 33.3 / 18.5	36.1 / 47.8 / 11.5 / 2.0		<0.001 / <0.001 / <0.001 / <0.001	30d mort higher, OS worse
Li, 2020[63]	Pancreas (low)	<80, ≥80	Any treatment / Surgery / Chemotherapy	78.7 / 43.0 / 63.9	44.5 / 17.9 / 29.7			Two-year OS worse
Metastatic setting								
Oytun, 2022[37]	Metastatic colon	<65, ≥65	Surgery / Adjuvant therapy / 1st line CT mono / No targeted therapy	44.9 / 22.3 / 2.4 / 29.5	35.3 / 16.2 / 10.4 / 53.2		0.042 / 0.113 / <0.001 / <0.001	Median OS lower, PFS similar
Liao, 2022[86]	Metastatic Gastric	≤70, >70	Pal. gastrectomy / Pal. chemotherapy	39.6 / 83.1	35.4 / 48.6		0.439 / <0.001	Median OS worse
Niedersüß-Beke, 2021[82]	Metastatic Colorectal	≤70, >70	Best Supportive care / Metastasis resection / Resection & systemic	11.2 / 9.5 / 21.0	35.7 / 7.9 / 9.1		<0.001 / 0.339 / <0.001	Median OS worse
Lemelin, 2020[85]	Metastatic Neuro-endocrine Tumors	<70, ≥70	Number treatments / Chemotherapy / Targeted therapy / Radionuclide	3.0 / 54 / 30 / 16	2.0 / 32 / 16 / 5		<0.0001 / <0.0001 / 0.0001 / <0.0001	Median OS worse

Table 2 (continued)

Part B. Age-related differences in treatment and outcomes for specific treatment-selected patients

Author, year	Site	Age	Treatment & outcomes	Young (%)	Middle (%)	Older 60+, 65+, 70+, 75+ (%)	Old 80+ (%)	p-value
SURGERY / TUMOR RESECTION								
Buonomo, 2023[11]	Breast (high)	45–70, ≥70	BCS for DCIS	79.0		86.7		0.298
			No complications	84.9		77.7		0.377
Luzarraga-Aznar, 2022[22]	Endometrial (high)	<75, ≥75	Adjuvant chemotherapy	30.6		16.5		0.014
			Adjuvant brachytherapy	31.7		17.5		0.016
			Adjuvant radiotherapy	19.0		10.3		0.062
			Complications	13.0		20.6		0.120
			5-year PFS	80.3		71.2		0.132
			5-year OS	80.1		50.1		<0.001
			5-year DSS	82.5		74.8		0.071
Matrone, 2020[111]	Thyroid (high)	<65, ≥65	Local treatments	11.2		6.4		0.17
			Systemic treatment	13.9		12.8		0.78
			Death rate 5 years	9.7		13.8		0.51
Inoue, 2019[108]	Hepato-cellular (high)	<80, ≥80	Complications	24.3			20.0	0.5879
			Mortality	5.8			8.9	0.3373
Shimada, 2020[107]	Hepato-cellular (high)	<65, 65–79, ≥80	30d mortality	0		0	0	0.86
			5-year OS	62		65	62	0.65
			Median RFS months	17		21	22	
Liu, 2021[109]	Liver (high)	<65, 65–74, ≥75	30-day mortality	1.3	1.0	1.1		0.9737
			Morbidity	39.0	39.4	58.5		0.0073
Cheng, 2022[41]	Colorectal (high)	65–79, ≥80	Complications			11.9	13.4	0.015
Kryzauskas, 2021[43]	Colorectal (high)	≤75, >75	Complications	29.7		37.0		0.066
			30d mortality	0.9		3.1		0.046
Cross, 2021[44]	Colorectal (high)	<80, ≥80	Adjuvant therapy colon/rectal	48/56			17/21	0.001
			Complications	13/11			23/25	<0.001
			30d mortality	0.9/0.4			3.3/3.1	<0.001
Sarasqueta, 2019[46]	Colorectal (high)	<65, 65–80, >80	Adjuvant CT colon	91.9	76.8		26.8	<0.0005
			Preop RT rectal	68.0	60.4		42.2	<0.0005
Ogata, 2022[40]	Colorectal (high)	<60, 60–79, ≥80	Post-operative mortality	0	0		2.5	0.072
			5-year survival	90.8	86.6		52.1	<0.001
Shafiei, 2020[38]	Colon (high)	≤69, 70–79, ≥80	Adjuvant chemotherapy	82.6		58.5	4.3	<0.001
Mazzola, 2023[36]	Colon (high)	<80, ≥80	Adjuvant chemotherapy	96.1			16.7	<0.001
			Overall complications	23.2			28.6	0.525
			Relapse	12.6			8.6	0.509
			Survival rate	79.3			67.7	0.183

Table 2 (continued)

Study	Cancer type	Age groups	Outcome	Value 1	Value 2	Value 3	p-value
Liu, 2023[109]	Colon (high)	<65, ≥65	Complications	24.9	37.7		<0.001
			OS 5-years	88.0	88.6		0.3
			DFS 5-years	89.7	90.5		0.38
Lee, 2022[105]	Gastro-intestinal (high)	<65, 65–79, ≥80	Surgical complications	39.7	46.5	13.9	0.265
			In hospital mortality	2.4	2.7	4.5	0.674
Leminski, 2022[89]	Bladder (low)	<70, ≥70	Neoadjuvant chemotherapy	18.61	17.58		0.772 0.353
			Complications (gr3-5)	25.31	29.09		0.175
			90d mortality	4.47	7.27		
			One-year mortality	33.25	46.67		0.003
Sirithanaphol, 2019[115]	Renal cell (low)	<65, ≥65	Open surgery	93.2	92.6		0.60
			90 days mortality	1.3	3.7		0.46
			Complications	12.2	22.2		0.21
			5-year survival	75.4	45.9		0.031
Joueidi, 2020[17]	Ovarian (low)	<65, 65–74, ≥75	Neoadjuvant chemotherapy	56	67	62	0.028
			<6 CT cycles	10	10	23	0.003
			DFS	47.2	33.7	37.2	0.057
			CSSS	81.7	67.3	57.4	<0.001
			OS	76.2	61.3	56.4	<0.001
Pinelli, 2021[18]	Ovarian (low)	<70, ≥70	Neoadjuvant chemotherapy	19	39		0.03
			Complete resection	78	87		0.32
			Complications	9	2		0.24
			Grade 3/4 AE	14	9		0.40
Laurent, 2022[52]	Esophageal (low)	<70, ≥70	Neo-adjuvant	61.5	44.3		0.018
			Adjuvant	41.7	23.0		0.004
			30d mortality	0.5	8.2		
Suzuki, 2022[55]	Esophageal (low)	<76, ≥76	Neoadjuvant chemo	77	55		0.001
			Completion rate NAC	85	71		0.116
			Grade 3 AE	27.5	42.9		0.091
Baranov, 2022[57]	Esophageal (low)	<75, ≥75	Neoadjuvant chemo	4.5	2.4		0.041
			Neoadjuvant CRT	88.6	88.6		0.990
			Open surgery	18.0	14.3		0.058
			Overall complications	61.5	67.9		0.032
			30d mortality	2.0	3.3		0.262
Kanda, 2019[53]	Esophageal (low)	<75, ≥75	Neoadjuvant therapy	47	42		0.562
			Adjuvant therapy	12	2		0.022
			Complications	12	8		0.445
Klevebro, 2019[58]	Esophageal or gastric (low)	<75, ≥75	Neoadjuvant CT gastric	60.7	8.3		0.691
			Neoadjuvant CT esophageal	25.0	4.8		0.421
			Complication esophageal	71.7	74.2		
			30d mortality esophageal	2.0	6.9		0.041
			Complication gastric	54.9	53.3		
			90d mortality gastric	7.6	18.6		0.028

Table 2 (continued)

Reference	Cancer type	Age groups	Outcome					p
Esaki, 2019[51]	Gastric (low)	<70, 70–79, ≥80	Additional surgery	70		54.7	20.1	0.001
Otowa, 2019[48]	Gastric (low)	≤69, 70–79, ≥80	Adjuvant chemotherapy	76.9		37.5	8.9	<0.001
			All complications	21.8		39.7	30.8	0.055
Komori, 2020[50]	Gastric (low)	<80, ≥80	Surgical complications	29.4			32.4	0.699
			Postoperative mortality	0.5			0	0.99
			5-year OS	66.7			59.6	0.103
			5-year CSS	78.2			67.9	0.028
Perla, 2021[118]	Infra-tentorial (low)	18–64, 65–74, ≥75	Any complication	8.07	15.07	21.94		<0.001
			30d mortality	1.07	3.18	6.45		0.019
Thakur, 2020[117]	Meningioma (low)	<65, ≥65	Radiation	16.2		6.7		0.053
			Major complication	8		8.7		0.62
Nia, 2020[121]	Mixed (craniotomy)	<65, ≥65	Major complications	6.59		9.23		<0.001
			Mortality	1.68		4.3		<0.001
De Leon, 2021[73]	Lung (low)	<65, ≥65	Open surgery	34		27		<0.03
			Complications	42		26		<0.001
Henry, 2022[65]	Pancreatic (low)	<75, ≥75	Neoadjuvant chemotherapy	8		5		0.11
			Adjuvant chemotherapy	69		37		<0.001
			Major complications	28		31		0.43
			90-day mortality	5		8		0.18
			OS months median	21		15		<0.001
			DFS months median	16		12		<0.001
Gruppo, 2020[61]	Pancreatic (low)	<75, ≥75	90-d mortality	1.4		9.1		0.088
			Complications	35.6		45.4		NS
			Mean OS months	28.5		22		0.909
Hackner, 2022[62]	Pancreatic (low)	≤70, >70	Adjuvant chemotherapy	60		46		0.038
			Major morbidity	24		33		0.167
			Mortality	2		7		0.073
			OS months	29.2		17.1		<0.001
			DFS months	14.9		10.4		0.034
Malik, 2020[70]	Pancreatic (low)	<70, ≥70	Neoadjuvant chemotherapy	5.5		3.2		0.524
			Adjuvant chemotherapy	61.7		47.9		0.040
			OS median	23.4		17.6		0.382
			DFS median	13.4		12.3		0.525
Ramanathan, 2019[60]	Pancreatic (low)	<60, 60–69, 70–79, ≥80	Mortality	0.29	0.59	0.58	0	0.7
Izumo, 2021[68]	Pancreatic (low)	<80, ≥80	Adjuvant chemotherapy	63			39	0.0085
			In hospital mortality	0.2			0	0.74
			Recurrence rate	72			61	0.64
			Median DSS years	2.8			2.3	0.47
			Median OS years	2.7			2.2	0.46

Table 2 (continued)

LAPAROSCOPIC OR ROBOTIC RESECTION

Study	Cancer (risk)	Age groups	Outcome	Group 1	Group 2	Group 3	Group 4	p
Hotton, 2020[21]	Endometrial (high)	<70, ≥70	No adjuvant treatment	43	32.2			NS
			Complications	10.5	12.9			NS
			Death	1.2	1.6			NS
Peltrini, 2021[24]	Rectal (high)	<75, ≥75	Complications	44.3	51.9			0.3
			Death during hospitalization	0.9%	0%			0.9
Xu, 2021[47]	Gastric (low)	<65, ≥65	Undergoing laparoscopic-assisted gastrectomy – complications	7.6	13.4			0.132

NEO-ADJUVANT THERAPY FOLLOWED BY SURGERY

Study	Cancer (risk)	Age groups	Outcome	Group 1	Group 2	Group 3	Group 4	p
Bongiolatti, 2020[123]	NSCLC (low)	<70, ≥70	Complications	38	46.1			0.47
			3-year OS	61	48.5			0.64
			2-year DFS	61.7	44			0.393
Liu, 2020[109]	Rectal (high)	<65, ≥65	Complications Neo-adj	12.67	21.36			0.099
			Complications surgery	13.70	8.74			P=0.189
Inanc, 2022[27]	Rectal (high)	<65, ≥65	Complications	0.8	3.3			0.058
			OS	79.0	68.0			0.05
			DFS	50.5	44.7			0.311
Sonal, 2023[25]	Rectal (high)	<70, ≥70	Complications	11.8	22.2			0.015
			Recurrence rate	17.9	13.1			0.284
			Mortality rate	14.4	44.4			<0.001
Cooper, 2021[54]	Esophageal (low)	<70, ≥70	Treatment completed	84	78			0.441
			Complications	49	58			0.222
			1-year mortality	9.6	17.3			0.2
Keywani, 2023[49]	Gastric (low)	<70, 70–74, 75–79, ≥80	Not proceed to surgery	77.3	64.0	62.4	68.4	<0.001
Oba, 2021[69]	Pancreatic (low)	<70, 70–74, ≥75	Surgical resection	80	50	35		<0.001
			Median survival months	23.6	18.0	17.6		0.090
Sawyer, 2021[67]	Pancreatic (low)	<70, 70–74, ≥75	Surgical resection	80	50	35		<0.001
			Side effects	19.4	14	12		0.563

NEO-ADJUVANT THERAPY FOLLOWED BY RADIOTHERAPY

Study	Cancer (risk)	Age groups	Outcome	Group 1	Group 2	Group 3	Group 4	p
Bryant, 2022[116]	Prostate (high)	≤59, 60–69, ≥70	Recurrence 10-y	35.0	31.8	26.7		<0.001
			PCa specific mortality	8.0	6.9	8.53		0.10

ADJUVANT CHEMOTHERAPY

Study	Cancer (risk)	Age groups	Outcome	Group 1	Group 2	Group 3	Group 4	p
Shiraishi, 2023[42]	Colorectal (high)	<70, ≥70	Adjuvant CT stage III	81.8	51.1			<0.001
			Complications surgery	28.9	23.4			0.383
Okamoto, 2022[45]	Colorectal (high)	<70, ≥70	Grade 3/4 AE	38	35			0.75
			Dose limiting toxicity	87	83			0.52
Hagerty, 2022[39]	Colon (high)	≤45, 50–75, >75	Adjuvant CT stage III	56	30	7		<0.001
Zambrano-Vera, 2021[19]	Ovarian (low)	<65, ≥65	Adjuvant CT Upfront	89.3	71.4			0.14
			NACT+CRS/HIPEC	95.2	70.4			0.03
			Salvage CT	66.7	36.8			0.03

Table 2 (continued)

ADJUVANT THERAPY

Author	Cancer type	Age groups	Parameter	Value 1	Value 2	Value 3	p-value
Matsuoka, 2021[124]	Bladder (low)	<75, ≥75	Receiving intravesical BCG after TURBT – 5-year RFS	51.6	59.4		0.72

RADIOTHERAPY

Author	Cancer type	Age groups	Parameter	Value 1	Value 2	Value 3	p-value
Hou, 202[13]	Cervical (high)	<70, ≥70	RT dose	80.4	70.3		0.002
			ICRT application	69.9	32.5		<0.001
			With chemotherapy	89.2	52.5		<0.001
			5-years OS	60.4	39.1		0.006
			5-years CSS	66.2	64.5		0.89
			5-years LRFS	82.6	82.1		0.91

IMMUNOTHERAPY

Author	Cancer type	Age groups	Parameter	Value 1	Value 2	Value 3	p-value
Nemoto, 2022[91]	Metastatic RCC (low)	≤70, >70	Nivo mono PFS median	5.69	7.3		0.607
			Nivo mono OS median	NR	31.1		0.383
			Nivo and Ipi PFS	9.70	6.08		0.997
			OS 1-year	82.8	86.6		0.714
Araujo, 2021[84]	Metastatic RCC (low)	<70, ≥70	OS months	30.8	25.1		<0.01
			Time treatment failure	6.9	6.9		0.4
Shiono, 2023[90]	SCLC (low)	<70, ≥70	Number cycles	2	2		0.81
			Median PFS months	4.9	5.5		0.18
			Median OS months	15.9	15.4		0.24
Okishio, 2020[76]	NSCLC (low)	<75, ≥75	Median doses	5	5		0.5074
			Median PFS months	2.1	2.1		0.5441
			OS median months	14.7	12.3		0.3272
Grosjean, 2021[74]	NSCLC (low)	<70, ≥70	Time to failure months	3.46	4.14		0.98
			Median OS	11.2	11.3		0.91
			Any significant AE	26.6	26.6		0.99
Galli, 2019[79]	NSCLC (low)	<70, 70–79, ≥80	Toxicity grade 2 or more	35.8	32.7	37.5	0.6493
			Median PFS months	2.8	3.5	2.6	0.2020
			Median OS months	9.1	11.3	9.6	0.5154
Vithayathil, 2022[92]	Hepatocellular (low)	<65, ≥65	OS months	15.1	14.9		0.67
			Median DFS	7.1	5.5		0.69
			Treatment related AE	73.3	62.1		0.11
Johns, 2021[120]	Mixed (low)	<70, ≥70	Any grade toxicity	28.7	36.1		0.05
			≥ Grade 3 toxicity	14.5	13.5		0.71

CHEMO-IMMUNOTHERAPY

Author	Cancer type	Age groups	Parameter	Value 1	Value 2	Value 3	p-value
Storm, 2022[122]	Mixed (low)	<65, ≥65	Chemo-immunotherapy Skin AE (most prevalent)	17.4	14.4		0.55
				45.7	60.0		0.036
Takeda, 2023[78]	SCLC (low)	<75, ≥75	Dose reduction	20.4	47.4		
			Median PFS months	5.1	5.5		
			Median OS months	14.1	12.0		

Table 2 (continued)

	Cancer	Age groups	Parameter				p
CHEMO-RADIOTHERAPY							
Zaborowska-Szmit, 2021[75]	NSCLC (low)	≤65, >65	Deterioration PS	31.3	15.4		0.03
			Complications G3/4	31.3	42.3		0.15
			Complete response	4.9	15.4		0.01
CHEMOTHERAPY							
Kotchetkov, 2023[93]	Lymphoma (low)	<70, ≥70	Full dose	79.5	44		<0.001
			Deaths	17.0	10.6		0.127
			DFS	27.3	22.1		0.401
Pilleron, 2023[77]	NSCLC (low)	<75, ≥75	Therapy adjusted	24	18		
			2 or more regimens	49	42–44		
			Median survival stage III	15.8	13.0		
			Median survival stage IV	7.7	7.9		
Potthoff, 2020[83]	Metastatic breast (low)	<70, ≥70	Time progression months	6.0	6.9		
			OS median months	16.4	14.5		
			AE (grade 3/4)	12.0	12.1		
Elias, 2022[64]	Metastatic pancreatic (low)	<70, 70–79, ≥80	First line treatment	74.9	70.9	58.4	<0.0001
			Second line treatment	43.0	34.5	26.7	<0.0001
			Third line treatment	34.4	31.3	31.5	0.3156
			Median OS months	7.9	6.8	6.2	<0.0001
Koga, 2022[81]	Metastatic pancreatic (low)	<75, ≥75	PFS	6.0	5.5		0.21
			OS	11.1	12.0		0.43
Kunkel, 2021[125]	Pancreatic (low)	<75, ≥75	Folfirinox	70.8	12.0		<0.001
			Gemcitabine mono Hemato-logic toxicity	38.9	72.0		0.004
				56.9	40.0		0.144
			Median survival months	12.7	9.9		0.001
Prager, 2021[80]	Pancreatic (low)	≤70, >70	Median PFS	5.562	5.520		0.81
			Median OS	10.64	10.22		0.4
			Adverse Drug Reaction	70.4	70.8		
TARGETED THERAPY							
Marta, 2021[106]	HCC (low)	<70, ≥70	Toxicities skin rash	38.5	33.3		0.532
			OS	8.0	9.0		0.433
			Time treatment failure	3.0	3.0		0.936

TN = triple negative, DCIS = ductal carcinoma in situ, BCS = breast conserving surgery, CT = chemotherapy, surg. = surgical, CSM = cancer specific mortality, pal. = palliative, MPM = Malignant pleural mesothelioma, LCNEC = large cell neuroendocrine carcinoma, RCC = Renal cell carcinoma, STS = Soft tissue sarcoma, OS = Overall Survival, CSS = cancer specific survival, RS = relative survival, mort. = mortality, NAC = neoadjuvant chemotherapy, AE = Adverse Events, CRT = chemoradiation, CT = chemotherapy, preop RT = preoperative radiotherapy, DFS = Disease Free Survival, DFS = Disease Free Survival, NSCLC = non-small cell lung cancer, SCLC = small cell lung cancer, Nivo = Nivolumab, and Ipi = ipilimumab

lead physician to rely on their assumptions and stereotypes [94–96].

Older patients are rarely included in randomized clinical trials. Reasons for their exclusion include comorbidities and polypharmacy, making it harder to meet clinical trial eligibility criteria; or the lack of physician knowledge about available trials or concerns about the potential risks and benefits of participation. Furthermore, beneficial treatment effects may be smaller in older patients with cancer due to specific aspects unique to this age group of patients, such as competing deaths, shorter follow-up, or compromised treatment tolerance [97]. Consequently, cancer treatment decisions for older adults are largely based on limited, post-hoc subgroup analyses and extrapolation of results from studies of younger patients [98]. While modified treatment strategies are frequently used for older patients, the evidence for such approaches is poor. Consequently, older adults are at higher risk of under and over treatment, which can affect their quality of life and survival [99]. Preferably, treatment decisions should consider physiological age, estimated life expectancy, risks, benefits, treatment tolerance, patient preferences, and potential treatment barriers [100]. There is growing evidence showing the effectiveness of comprehensive geriatric assessment together with targeted intervention to improve quality of life, reduce the risk of toxicity and complications. This is also recommended by the American Society of Clinical Oncology and the International Society for Geriatric Oncology [101, 102].There is a crucial need for a better representation of older adults in cancer research and observational studies are an important data sources to fill the gap in evidence.

Consistently, older patients selected for treatment have similar outcomes than younger patients, suggesting the appropriate selection of patients for treatment. However, this is not conclusive with respect to the patients who were not selected for treatment but could have benefited from it. It is likely that those older adults who received treatment were fitter than those who did not. Information on frailty status would be valuable to better describe older patients who received treatment compared to those who did not. However, such information is rarely available routinely in observational studies [103]. Fortunately, some tools are being developed to assess frailty in secondary health data [104].

Most studies compared overall survival between younger and older adults; however, older adults have a higher baseline mortality than younger adults. While overall survival in patients with cancer can provide valuable information over short periods, it may not be the most relevant metric for long-term comparisons across age groups as it does not make the distinction between the cause of death. Cancer-specific survival in hospital settings, where the cause of death can be accurately determined, or net survival metrics in population-based studies, where the cause of death may be less reliable, could be better options. These metrics remove the effect of population mortality, making them more suitable for comparing survival between older and younger age groups.

The observational studies included are descriptive studies, and not designed to compare treatment effectiveness. Evaluating treatment effectiveness using observational is complicated by the inherent biases of observational studies such as selection or confounding which can affect interpretation. Such studies require special attention when planning the study, analyzing data and interpreting results; well-thought observational studies in older patients with cancer are urgently needed to fill the knowledge gaps.

Limitations of the present review are the strict selection criteria and the reduction in the items that were extracted from the articles. Moreover, the different definitions and cut-offs used in the articles complicated the overview (both age categories and the outcomes). Most of the selected articles were from European or USA data, highlighting the importance of much needed research from other parts of the world. Besides, most of the studies were performed in a single center; therefore informative larger population-based studies are warranted to reduce the risk of selection bias. Last, for the aim of this overview, we had to select items to extract from the articles, thereby acknowledging that some important items and outcomes such as quality of life or functional outcomes are missing in this systematic review.

Conclusion

Older patients continue to receive less treatment and have poorer survival compared to their younger counterparts, with more pronounced differences in patients over the age of 80. However, older patients selected for specific treatments experienced comparable complications and adverse events rates as well as similar survival. Given the lack of evidence to tailor treatment for older patients with cancer, it is crucial to increase their representation in clinical trials; this is particularly important for evaluating different treatment options in the oldest and frailest patients.

Key References

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  ○ This study with the National Cancer Database compares treatment of younger and older patients with triple-negative breast cancer.

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Data Availability No datasets were generated or analysed during the current study.

Declarations

Conflicts of Interest The authors declare no competing interests.

Human and Animal Rights This article does not contain any studies with human or animal subjects performed by any of the authors.

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