CO208

Recurrence rates and survival among patients with early-stage cancers: A systematic literature review

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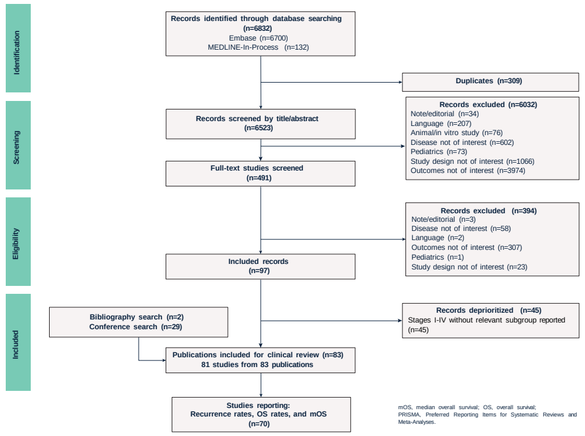
Objectives

- Following treatment, many patients experience recurrence of their cancer over time, resulting in a detrimental impact on patients and health systems. However, the frequency of recurrences is not well understood across different early-stage tumors
- A narrative systematic literature review was conducted to assess the recurrence rates and overall survival (OS) of patients diagnosed with early-stage cancers

Methods

- The systematic literature search was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [PRISMA] methodology
- The Embase® and MEDLINE® databases were searched to identify observational studies, published in English between May 2012 and May 2022, that reported recurrence rates and OS among adult patients with bladder cancer (BLA), gastric cancer (GC), head and neck cancer (HNC), melanoma (MEL), non-small cell lung cancer (NSCLC), renal-cell carcinoma (RCC), and triple- negative breast cancer (TNBC)
- Titles/abstracts of the identified literature were first screened to select potentially relevant studies, followed by full-text screening to define the final list for inclusion. At each stage, 2 independent reviewers conducted the initial screening, with discrepancies being resolved by a third independent reviewer

Figure 1. PRISMA flow diagram



mOS, median overall survival; OS, overall survival; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Results

- Among the selected studies in the clinical review (n=81), studies that reported recurrence rate, median OS (mOS), and OS rate data were primarily identified for patients with BLA (n=19), HNC (n=6), MEL (n=20), and TNBC (n=16). Limited evidence was available for patients with NSCLC (n=7) and RCC (n=2), and no evidence was available for GC (**Figure 1**)

Table 1. Summary of recurrence rates by tumor type and stage at diagnosis

Tumor type	Early-stage criteria defined in SLR	Stage at diagnosis	Recurrence rates (%)
BLA	Stages I to III, excluding unresectable Stage III (muscle invasive and nonmuscle invasive)	Ta	28.0-78.0[1-3]
		Ta low grade	35.9-53.4[4-6]
		Ta high grade	35.9-70.1[4,7]
		Tis	70.6[7]
		T1a-c	75-88[8]
		Low-grade T1	46.8[4]
		High-grade T1	34.5-77.2[4,7,9,10]
		Poorly differentiated	74.2[7]
		Undifferentiated	74.5[7]
GC	Patients diagnosed with early gastric cancer/gastroesophageal junction, Stages I-IVA	N/A	N/A
HNC	Head and neck cancer (Stages I-IVA, including locally advanced)	Stage 0-I	13-13.4[11,12]
		Stage II	22-32.4[11,12]
		Stage III	25-34.2[11,12]
		T1	13.5-16.6[12-14]
		T2	22.7-44.4[12-14]
		T3	24.7-69.2[12-14]
MEL	Stages I to III, excluding unresectable Stage III	Stage I	14.6[15]
		Stage IB	5.5-8.0[16,17]
		Stage II	14.5-29.0[15,16,18]
		Stage IIA	13.6-16.9[17,18]
		Stage IIB	19.1-94.7[17-19,23]
		Stage IIC	24.4-100[17-19,23]
		Stage III	22.6-67.6[15,16,20-22]
		Stage IIIA	46.5-83.3[19,23]
		Stage IIIB	88.9[19]
		Stage IIIC	97.1[19]
NSCLC	NSCLC (squamous and nonsquamous), including: -Surgically treated early-stage patients with Stage IB-IIIA NSCLC (AJCC V7), corresponding to Stage II, IIIA, and resectable IIIB (T3-4N2) NSCLC (AJCC V8) -Surgically ineligible early-stage patients receiving radiation therapy in Stage I or II (T1 to limited T3, N0, M0) NSCLC (AJCC V8)	Stage I	22-36[24]
		Stage IA	10[25]
		Stage IB	0a-20[25,26]
		Stage IIA	22.3-50[25,26][8]
		Stage IIB	25.5-39[25,26]
		Stage III	67[27]
		Stage IIIA	31.2-70.8[25-27]
		Stage IIIB	73.8-100[25,27][8]
		Stage I-III	30[28]
RCC	RCC (Stages I-IV; T1-T4, N0/M0)	T1a	5.4[29]
		T1b	15.3[29]
		T2	25.7[29]
		T3	42.1[29]
		Fuhrman grade G1	6.3[29]
		Fuhrman grade G2	13.3[29]
		Fuhrman grade G3	31.7[29]
		Fuhrman grade G4	55.2[29]
		Fuhrman grade GX	23.5[29]
TNBC	Stages I to III, excluding unresectable Stage III	Stage I	16.4-30.2[30,31]
		Stage II	26.8-69.8[30,31]
		Stage III	53.7[31]

N/A, not available. aRecurrence rate value out of <10 patients assessed within subgroup.

Recurrence rates by tumor type and stage at diagnosis

- Availability of data for recurrence rates according to stage of disease at initial diagnosis varied by tumor type, as well as across patient subgroups within each type of cancer (**Table 1**)
- An overall trend was observed for increased likelihood of recurrence in patients diagnosed with more-advanced stages of disease vs earlier stages of disease. However, similar values were reported among some patient subpopulations, suggestive of comparable risk of recurrence among some patient subgroups despite differing stages of disease at diagnosis, including BLA: poorly differentiated vs undifferentiated; HNC: Stage II vs Stage III and T2 vs T3; MEL: Stage IIC vs Stage III; RCC: T1a vs T1b

Recurrence-related survival by tumor type and stage at diagnosis

- Among the selected studies, reporting of OS data in patients experiencing recurrence after an initial diagnosis of early-stage disease was sparse (**Table 2**)
- Where available, mOS was the most commonly reported endpoint, although there was substantial heterogeneity among the patient subpopulations investigated
- Indicators for improved overall survival included an absence of progression (vs disease progression), earlier stage of disease at initial diagnosis (vs later stage), and locoregional recurrence (vs distant metastases). In TNBC, brain metastases were associated with reduced mOS vs other distant metastases

Table 2. Summary of recurrence-related OS data by tumor type and stage at diagnosis

Tumor type	Patient population		Endpoints			
	Stage and subtype of disease	Recurrence status	mOS (months)	1-year OS (%)	3-year OS (%)	5-year OS (%)
BLA	NMIBC: T1 high-grade	With progression	18.2[10]	-	-	43.75[10]
		Without progression	45.2[10]	-	-	84.73[10]
GC	-	-	-	-	-	-
HNC	-	-	-	-	-	-
MEL	Stages I-II	Late recurrence	31[32]	71.9[32]	44.3[32]	37.5[33]
		Early recurrence (early metastasis)	32[32]	72.4[32]	47.2[32]	39.3[33]
	Stages I-III	Postrecurrence	10.5-27[22,34]	-	-	-
		Regional lymph node metastases	46.8[16]	-	-	-
		Intralymphatic metastases	33.6[16]	-	-	-
	Stages I-III	Locoregional recurrence	16.5[22]	-	-	-
		Mixed locoregional and distant	6[22]	-	-	-
		Distant alone	6[22]	-	-	-
	Cutaneous melanoma: Stage I-III	Postlocoregional metastasis melanoma-specific survival	53.76[35]	-	-	-
		Postmixed recurrence melanoma-specific survival	11.76[35]	-	-	-
		Postdistant metastasis melanoma-specific survival	10.92[35]	-	-	-
	Cutaneous melanoma: Stage I	Postrecurrence melanoma-specific survival	29.04[35]	-	-	88.2[15]
	Cutaneous melanoma: Stage IB	Postrecurrence melanoma-specific survival	22.8[16]			
	Cutaneous melanoma: Stage II	Postrecurrence melanoma-specific survival	18-27.24[16,35]	-	-	75.1[15]
	Cutaneous melanoma: Stage III	Postrecurrence melanoma-specific survival	13.2-20.4[16,35]	-	-	42.9[15]
NSCLC	-	-	-	-	-	-
RCC	-	-	-	-	-	-
TNBC	Stage I	Post-brain metastases	7.7[36]			
	Stage II	Post-brain metastases	9.8[36]			
	Stage III	Post-brain metastases	5.8[36]			
	Stages I-III	Post-brain metastases	7.2[36]			
		After other distant metastases	11.6[36]			

mOS, median overall survival; N/A, not available; NMIBC, nonmuscle invasive bladder cancer; OS, overall survival.

Conclusions

- Even after treatment with standard treatment options, many patients diagnosed with early-stage cancers are still at high risk of recurrence. Recurrences are life altering for patients, and survival is negatively affected for patients experiencing recurrences, especially those of the metastatic type. This suggests that there is an unmet need for effective therapies in the neoadjuvant and adjuvant settings
- Overall, patients diagnosed at earlier stages of disease experienced lower recurrence rates than those diagnosed at later stages of disease. Among patients who experienced recurrence, those with locoregional recurrence had improved OS compared to those with distant metastases

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