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Characteristics and patient-reported outcomes of long-term cancer survivors after apatinib-based therapy: an online survey

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Abstract

Background Data on long-term cancer survivors treated with apatinib are lacking. This study aimed to describe the characteristics of long-term cancer survivors after apatinib-based therapy, and to know about their satisfaction degree with apatinib and severity of depression and insomnia.

Methods Patients with solid tumors who had received apatinib-based therapy for at least 5 years were invited to complete an online questionnaire. Characteristics of patients and treatment, knowledge of apatinib, satisfaction degree, and severity of depression and insomnia assessed by Patient Health Questionnaire-9 and Insomnia Severity Index were collected.

Results Between December 8, 2023 and March 1, 2024, a total of 436 patients completed the online questionnaire. Most patients were satisfied with the efficacy (96.6%) and safety (93.1%) of apatinib, were willing to continue apatinib treatment (99.5%), and would recommend apatinib to other patients (93.3%). Continuous apatinib treatment resulted in significant negative impact on daily life, work, or study in only two (0.5%) patients. Almost all patients currently had no or mild depression (97.0%) and insomnia (97.9%) problems. The most common patient-reported adverse events were hand-foot syndrome (21.3%) and hypertension (18.3%).

Conclusions Our survey showed a high satisfaction degree with apatinib in long-term cancer survivors. Long-term apatinib treatment resulted in almost no negative impact on patient's quality of life.

Keywords Apatinib, Cancer, Depression, Insomnia, Survey

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Introduction

Cancer is one of the leading causes of death, and the cancer burden is rapidly growing worldwide. Globally, there were 19.29 million newly-diagnosed cases and 9.96 million cancer deaths in 2020, and Asia accounted for 49.3% of these new cases and 58.3% of cancer deaths [1]. With the great evolution of anti-cancer therapies (including chemotherapy, radiotherapy, surgery, targeted therapy, and immunotherapy) over the past few decades, increase in 5-year survival rate has been observed across almost all tumor types in different countries [2–5]. For long-term cancer survivors, the improvement in quality of life is an essential dimension when they consider whether to continue the original treatment regimen or switch to a new one.

Depression and insomnia are two common comorbidities of cancer. Approximately 10-15% of patients with cancer have major depression [6, 7], and the prevalence of insomnia syndrome is 21-35% during anti-cancer therapy [8, 9]. These two disorders largely affect patient's ability to work and study, social activities, leading to dissatisfaction and poor compliance to treatment. Thus, the impact on mood and sleep is an important aspect to assess the advantages of an anti-cancer drug.

Apatinib is an oral small-molecule tyrosine kinase inhibitor targeting vascular endothelial growth factor receptor 2. It has been approved for the treatment of advanced gastric cancer and hepatocellular carcinoma in China [10–13], and has shown clinical benefits in other solid tumors based on results from phase 3 trials [14–16]. However, studies focusing on long-term survivors treated with apatinib, and corresponding data on depression and insomnia are scarce.

Here we aimed to describe the characteristics of long-term cancer survivors after apatinib-based therapy, and to know about their satisfaction degree with apatinib and severity of depression and insomnia.

Methods

Study design and patients

This was a cross-sectional study conducted at 279 centers across China. Patients with solid tumors who had received apatinib-based therapy for at least 5 years and could understand the contents of our questionnaire were eligible for this study. The study was approved by the ethics committee of the Peking University International Hospital and all other participating centers. Written informed consent was obtained from each patient before participating in this survey.

Questionnaire

Patients were invited to complete an online questionnaire when they came to the outpatient department. There was no compensation for patients participating in this survey. The questionnaire was developed for this study, which consisted of three parts (Additional file 1). The first part collected the characteristics of patients and treatment, including birth date, sex, cancer type, date of the first diagnosis, disease status at diagnosis (operable or inoperable disease), history of cancer surgery, date of initiating apatinib-based therapy, initial and current dose of apatinib, reason for dose reduction, combined anti-cancer drug when initiating apatinib treatment, and patient-reported adverse events (AEs). In the second part, patients answered 8 questions to reflect their knowledge of apatinib and satisfaction degree. The third part assessed the severity of depression and insomnia using Patient Health Questionnaire (PHQ)-9 and Insomnia Severity Index (ISI).

PHQ-9 is a 9-item tool for the screening of depression [17]. The score of each item ranges from 0 to 3, with a total score of 0–27. Higher PHQ-9 score indicates greater depression severity, with 0–4 regarded as minimal depression, 5–9 as mild depression, 10–14 as moderate depression, 15–19 as moderately severe depression, and 20–27 as severe depression. ISI can be used to evaluate insomnia symptoms, which consists of seven items [18]. Each item is rated on a 0–4 Likert scale, with a total score of 0–28. Higher ISI score indicates greater insomnia severity, with 0–7 regarded as no clinically significant insomnia, 8–14 as subthreshold insomnia, 15–21 as moderate insomnia, and 22–28 as severe insomnia.

Statistical analysis

All the statistical analyses were descriptive, performed using SAS version 9.4. Continuous variables were expressed as median (range), and categorical variables were expressed as frequency (percentage).

Results

Patient characteristics

Between December 8, 2023 and March 1, 2024, a total of 436 patients completed the online questionnaire. The median age at diagnosis was 51 years (range, 11–80), and the median disease duration was 7.0 years (range, 5.2–21.8). The majority of patients were males (61.2%), had operable disease at diagnosis (81.9%), and had prior cancer surgery (76.1%). Among these patients, 125 (28.7%) had liver cancer, 90 (20.6%) had gastric cancer, 44 (10.1%) had lung cancer, 32 (7.3%) had sarcoma, 28 (6.4%) had ovarian cancer, 27 (6.2%) had thyroid cancer, and 90 (20.6%) had other tumors (Table 1).

Treatment characteristics

The majority of 436 patients received apatinib-based therapy for the treatment of advanced disease (83.7%). The most common initial dose of apatinib was 500 mg/day (52.3%), followed by 250 mg/day (37.6%). The most

Table 1 Patient characteristics

Characteristics	Total (*n* = 436)	Liver cancer (*n* = 125)	Gastric cancer (*n* = 90)	Lung cancer (*n* = 44)	Sarcoma (*n* = 32)	Ovarian cancer (*n* = 28)	Thyroid cancer (*n* = 27)	Others (*n* = 90)
Age at diagnosis (years), median (range)	51 (11–80)	51 (26–71)	53 (19–78)	52 (14–80)	25 (11–68)	49 (33–64)	47 (18–77)	50 (14–74)
<65	402 (92.2)	117 (93.6)	78 (86.7)	39 (88.6)	31 (96.9)	28 (100)	25 (92.6)	84 (93.3)
≥65	34 (7.8)	8 (6.4)	12 (13.3)	5 (11.4)	1 (3.1)	0	2 (7.4)	6 (6.7)
Sex								
Male	267 (61.2)	111 (88.8)	66 (73.3)	22 (50.0)	15 (46.9)	0	13 (48.1)	40 (44.4)
Female	169 (38.8)	14 (11.2)	24 (26.7)	22 (50.0)	17 (53.1)	28 (100)	14 (51.9)	50 (55.6)
Disease status at diagnosis								
Operable	357 (81.9)	104 (83.2)	83 (92.2)	22 (50.0)	26 (81.3)	24 (85.7)	25 (92.6)	73 (81.1)
Inoperable	79 (18.1)	21 (16.8)	7 (7.8)	22 (50.0)	6 (18.8)	4 (14.3)	2 (7.4)	17 (18.9)
Disease duration (years), median (range)	7.0 (5.2–21.8)	6.5 (5.2–15.6)	7.0 (5.3–14.7)	7.4 (5.6–16.8)	6.9 (5.4–21.8)	7.3 (5.7–13.7)	8.9 (5.2–17.1)	7.6 (5.2–17.5)
Prior cancer surgery								
Yes	332 (76.1)	97 (77.6)	80 (88.9)	19 (43.2)	22 (68.8)	24 (85.7)	22 (81.5)	68 (75.6)
No	104 (23.9)	28 (22.4)	10 (11.1)	25 (56.8)	10 (31.3)	4 (14.3)	5 (18.5)	22 (24.4)

Data are *n* (%), unless otherwise indicated

common current dose was 250 mg/day (45.6%), followed by 500 mg/day (38.5%) and 125 mg/day (6.4%). Dose reduction due to AEs occurred in 22.7% of patients, while 72.7% of patients had no dose reduction of apatinib. Most patients (55.7%) received apatinib monotherapy, while apatinib combined with chemotherapy was administered in 6.2% of patients. The median duration of apatinib treatment was 6.2 years (range, 5.0–10.0; Table 2).

Patient's knowledge of apatinib and satisfaction degree

The majority of 436 patients were aware of the standard treatment options for their disease (84.4%), and the mechanism of action and possible side effects of apatinib (91.3%). Of these patients, 51.1% received apatinib based on doctor's choice, while 43.6% selected apatinib due to its efficacy. Almost all patients were satisfied with the efficacy (96.6%) and safety (93.1%) of apatinib, and were willing to continue apatinib treatment in the future (99.5%). Continuous apatinib treatment resulted in significant negative impact on daily life, work, or study in only two (0.5%) patients, a certain negative impact in 20.6% of patients, and little or no negative impact on 67.4% of patients. Most patients (93.3%) would recommend apatinib to other patients (Table 3).

Depression and insomnia

After at least 5 years of apatinib treatment, four (0.9%) of 436 patients had moderate depression, eight (1.8%) had moderately severe depression, and only one (0.2%) had severe depression. Nine (2.1%) patients had moderate insomnia, and no patients had severe insomnia (Fig. 1).

Patient-reported AEs

Of 436 patients, 44.7% reported at least one AE. The most common patient-reported AEs were hand-foot syndrome (21.3%), hypertension (18.3%), proteinuria (4.6%), and diarrhea (3.4%; Table 4).

The incidence of patient-reported AEs was 40.2% in 164 patients with apatinib 250 mg/day, 48.2% in 228 patients with apatinib 500 mg/day, 41.6% in 243 patients with apatinib monotherapy, and 56.1% in 66 patients with apatinib-based combination therapy. The most common patient-reported AEs were hand-foot syndrome and hypertension in all these subgroups (Additional file 2: Supplementary Table 1).

Discussion

This study summarized the demography, disease, and treatment characteristics of patients with various types of solid tumor who had been treated with apatinib-based therapy for at least 5 years through an online survey. Knowledge of apatinib, satisfaction degree with apatinib treatment, and severity of depression and insomnia were also assessed in this population. Most patients were aware of the standard treatment for their disease (84.4%) and apatinib (91.3%). Over 93% of patients were satisfied with apatinib treatment, were willing to continue it, and would recommend apatinib to other patients. Only 0.5% of patients suffered significant negative impact on daily life, work, or study during apatinib-based therapy. Almost all patients currently had no or mild depression (97.0%) and insomnia (97.9%) problems. The safety profile reported by patients were acceptable. All these data demonstrated the favorable impression made by apatinib on long-term cancer survivors.

Table 2 Treatment characteristics

Characteristics	Total (*n* = 436)	Liver cancer (*n* = 125)	Gastric cancer (*n* = 90)	Lung cancer (*n* = 44)	Sarcoma (*n* = 32)	Ovarian cancer (*n* = 28)	Thyroid cancer (*n* = 27)	Others (*n* = 90)
Apatinib treatment setting								
As adjuvant therapy[a]	46 (10.6)	23 (18.4)	14 (15.6)	1 (2.3)	4 (12.5)	1 (3.6)	0	3 (3.3)
For advanced disease	365 (83.7)	95 (76.0)	73 (81.1)	40 (90.9)	24 (75.0)	27 (96.4)	24 (88.9)	82 (91.1)
Unknown	25 (5.7)	7 (5.6)	3 (3.3)	3 (6.8)	4 (12.5)	0	3 (11.1)	5 (5.6)
Initial dose (mg/day)								
125	3 (0.7)	1 (0.8)	0	1 (2.3)	0	1 (3.6)	0	0
250	164 (37.6)	51 (40.8)	23 (25.6)	23 (52.3)	6 (18.8)	17 (60.7)	8 (29.6)	36 (40.0)
375	6 (1.4)	1 (0.8)	0	0	2 (6.3)	0	1 (3.7)	2 (2.2)
425	5 (1.1)	1 (0.8)	0	0	1 (3.1)	0	1 (3.7)	2 (2.2)
500	228 (52.3)	63 (50.4)	48 (53.3)	19 (43.2)	22 (68.8)	10 (35.7)	17 (63.0)	49 (54.4)
675	1 (0.2)	1 (0.8)	0	0	0	0	0	0
750	19 (4.4)	3 (2.4)	15 (16.7)	1 (2.3)	0	0	0	0
850	10 (2.3)	4 (3.2)	4 (4.4)	0	1 (3.1)	0	0	1 (1.1)
Current dose (mg/day)								
125	28 (6.4)	7 (5.6)	2 (2.2)	3 (6.8)	0	7 (25.0)	2 (7.4)	7 (7.8)
250	199 (45.6)	62 (49.6)	29 (32.2)	25 (56.8)	12 (37.5)	12 (42.9)	14 (51.9)	45 (50.0)
375	17 (3.9)	4 (3.2)	1 (1.1)	1 (2.3)	4 (12.5)	0	3 (11.1)	4 (4.4)
500	168 (38.5)	47 (37.6)	44 (48.9)	14 (31.8)	15 (46.9)	8 (28.6)	7 (25.9)	33 (36.7)
675	2 (0.5)	1 (0.8)	0	0	0	0	1 (3.7)	0
750	18 (4.1)	2 (1.6)	13 (14.4)	1 (2.3)	1 (3.1)	0	0	1 (1.1)
850	3 (0.7)	2 (1.6)	1 (1.1)	0	0	0	0	0
Unfixed dose	1 (0.2)[b]	0	0	0	0	1 (3.6)[b]	0	0
Reason for dose reduction								
Adverse event	99 (22.7)	26 (20.8)	12 (13.3)	8 (18.2)	9 (28.1)	10 (35.7)	10 (37.0)	24 (26.7)
Patient's decision	1 (0.2)	0	0	1 (2.3)	0	0	0	0
Doctor's decision	19 (4.4)	8 (6.4)	5 (5.6)	0	2 (6.3)	0	2 (7.4)	2 (2.2)
No dose reduction	317 (72.7)	91 (72.8)	73 (81.1)	35 (79.5)	21 (65.6)	18 (64.3)	15 (55.6)	64 (71.1)
Combined anti-cancer drug at initiation of apatinib								
Immunotherapy	13 (3.0)	4 (3.2)	1 (1.1)	3 (6.8)	0	3 (10.7)	0	2 (2.2)
Targeted therapy	8 (1.8)	0	0	6 (13.6)	1 (3.1)	1 (3.6)	0	0
Chemotherapy	27 (6.2)	4 (3.2)	6 (6.7)	3 (6.8)	1 (3.1)	3 (10.7)	1 (3.7)	9 (10.0)
Traditional Chinese medicine	15 (3.4)	7 (5.6)	3 (3.3)	2 (4.5)	0	0	0	3 (3.3)
Others	4 (0.9)	2 (1.6)	0	1 (2.3)	0	0	0	1 (1.1)
None	243 (55.7)	59 (47.2)	56 (62.2)	21 (47.7)	22 (68.8)	18 (64.3)	16 (59.3)	51 (56.7)
Unknown[c]	127 (29.1)	49 (39.2)	24 (26.7)	8 (18.2)	8 (25.0)	4 (14.3)	10 (37.0)	24 (26.7)
Duration of apatinib treatment (years), median (range)	6.2 (5.0–10.0)	5.9 (5.0-8.9)	6.4 (5.0–10.0)	6.4 (5.1–8.1)	6.2 (5.0-9.2)	6.0 (5.2–8.8)	6.5 (5.2–8.2)	6.1 (5.0-9.2)

Data are *n* (%), unless otherwise indicated

[a] Apatinib was deemed as adjuvant therapy when used within 1 month after surgery

[b] One patient with ovarian cancer adjusted the dose of apatinib by herself based on adverse reactions

[c] Patients forgot their combined anti-cancer drug at initiation of apatinib when they filled the questionnaire

In our study, the most common initial dose of apatinib was 500 mg/day (52.3%), followed by 250 mg/day (37.6%). In real world, these two doses are indeed commonly used for patients [19–21]. When apatinib is prescribed as monotherapy or a part of combination therapy, the recommended dose is 500 mg/day and 250 mg/day, respectively, as supported by safety and dose adjustment data from previous pivotal clinical trials [10–16]. Even for advanced gastric cancer, 90% of patients were prescribed at an initial dose of 500 mg/day rather than the approved dose of 850 mg/day according to the results from the phase 4 AHEAD study of 1999 patients [22]. Thus, our data are in line with expectation.

We found that most patients knew about the standard treatment for their disease and apatinib. In addition to patient education, the current information era has provided many modern approaches for patients to learn disease knowledge, search treatment guidelines and corresponding literatures, and obtain information they need on the internet. This can be reflected by the questionnaire

Table 3 Patient's knowledge of apatinib and satisfaction degree

Item	Total (*n* = 436)	Liver cancer (*n* = 125)	Gastric cancer (*n* = 90)	Lung cancer (*n* = 44)	Sarcoma (*n* = 32)	Ovarian cancer (*n* = 28)	Thyroid cancer (*n* = 27)	Others (*n* = 90)
Are you aware of the standard treatment options for your disease?								
Very clear	98 (22.5)	28 (22.4)	21 (23.3)	10 (22.7)	3 (9.4)	6 (21.4)	5 (18.5)	25 (27.8)
Generally aware	270 (61.9)	76 (60.8)	51 (56.7)	29 (65.9)	24 (75.0)	19 (67.9)	20 (74.1)	51 (56.7)
Not clear	68 (15.6)	21 (16.8)	18 (20.0)	5 (11.4)	5 (15.6)	3 (10.7)	2 (7.4)	14 (15.6)
Are you aware of the mechanism of action and possible side effects of apatinib?								
Very clear	112 (25.7)	26 (20.8)	26 (28.9)	13 (29.5)	8 (25.0)	6 (21.4)	7 (25.9)	26 (28.9)
Generally aware	286 (65.6)	90 (72.0)	51 (56.7)	26 (59.1)	22 (68.8)	21 (75.0)	19 (70.4)	57 (63.3)
Not clear	38 (8.7)	9 (7.2)	13 (14.4)	5 (11.4)	2 (6.3)	1 (3.6)	1 (3.7)	7 (7.8)
What was the main reason for choosing apatinib?								
Efficacy	190 (43.6)	58 (46.4)	37 (41.1)	24 (54.5)	13 (40.6)	16 (57.1)	11 (40.7)	31 (34.4)
Safety	9 (2.1)	3 (2.4)	3 (3.3)	0	1 (3.1)	0	0	2 (2.2)
Financial reasons	14 (3.2)	7 (5.6)	1 (1.1)	1 (2.3)	1 (3.1)	0	1 (3.7)	3 (3.3)
Doctor's choice	223 (51.1)	57 (45.6)	49 (54.4)	19 (43.2)	17 (53.1)	12 (42.9)	15 (55.6)	54 (60.0)
How satisfied are you with the efficacy of apatinib?								
Very satisfied	217 (49.8)	67 (53.6)	48 (53.3)	19 (43.2)	14 (43.8)	11 (39.3)	13 (48.1)	45 (50.0)
Satisfied	204 (46.8)	55 (44.0)	41 (45.6)	23 (52.3)	15 (46.9)	16 (57.1)	12 (44.4)	42 (46.7)
Neutral	12 (2.8)	1 (0.8)	1 (1.1)	2 (4.5)	3 (9.4)	1 (3.6)	2 (7.4)	2 (2.2)
Dissatisfied	1 (0.2)	1 (0.8)	0	0	0	0	0	0
Very dissatisfied	2 (0.5)	1 (0.8)	0	0	0	0	0	1 (1.1)
How satisfied are you with the safety of apatinib?								
Very satisfied	187 (42.9)	56 (44.8)	41 (45.6)	16 (36.4)	12 (37.5)	10 (35.7)	11 (40.7)	41 (45.6)
Satisfied	219 (50.2)	65 (52.0)	43 (47.8)	25 (56.8)	17 (53.1)	17 (60.7)	12 (44.4)	40 (44.4)
Neutral	27 (6.2)	4 (3.2)	6 (6.7)	2 (4.5)	3 (9.4)	1 (3.6)	3 (11.1)	8 (8.9)
Dissatisfied	1 (0.2)	0	0	0	0	0	1 (3.7)	0
Very dissatisfied	2 (0.5)	0	0	1 (2.3)	0	0	0	1 (1.1)
To what extent has the continuous use of apatinib negatively impacted your daily life/work/study?								
No impact at all	112 (25.7)	30 (24.0)	29 (32.2)	11 (25.0)	7 (21.9)	7 (25.0)	8 (29.6)	20 (22.2)
Little impact	182 (41.7)	54 (43.2)	42 (46.7)	19 (43.2)	10 (31.3)	12 (42.9)	6 (22.2)	39 (43.3)
Neutral	50 (11.5)	15 (12.0)	7 (7.8)	2 (4.5)	7 (21.9)	4 (14.3)	3 (11.1)	12 (13.3)
A certain impact	90 (20.6)	25 (20.0)	12 (13.3)	12 (27.3)	8 (25.0)	5 (17.9)	9 (33.3)	19 (21.1)
Significant impact	2 (0.5)	1 (0.8)	0	0	0	0	1 (3.7)	0
Will you continue to use apatinib in the future?								
Yes	434 (99.5)	124 (99.2)	89 (98.9)	44 (100)	32 (100)	28 (100)	27 (100)	90 (100)
No	2 (0.5)	1 (0.8)	1 (1.1)	0	0	0	0	0
Will you recommend apatinib to other patients?								
Yes	407 (93.3)	119 (95.2)	82 (91.1)	40 (90.9)	27 (84.4)	28 (100)	25 (92.6)	86 (95.6)
No	29 (6.7)	6 (4.8)	8 (8.9)	4 (9.1)	5 (15.6)	0	2 (7.4)	4 (4.4)

Data are *n* (%)

data that 43.6% of patients selected apatinib due to its efficacy rather than doctor's choice. However, the selection of treatment regimen is just the first step. The real reason why patients persist in using the same drug must be due to its long-term efficacy, safety, and positive impact on quality of life. In our study, all patients had been treated with apatinib for a median of 6.2 years. Over 93% of patients were satisfied with both the efficacy and safety of apatinib, were willing to continue it, and would recommend apatinib to other patients. These results indicate a high level of patient acceptance for long-term use of apatinib. In addition, continuous apatinib treatment led to significant negative impact on daily life, work, or study in only 0.5% of patients. No more than 3.0% of patients had moderate or greater depression or insomnia after at least 5 years of apatinib treatment. As an oral drug, it is also convenient for patients to take apatinib, without concern about frequent visit to hospitals. These results suggest that apatinib has almost no long-term negative impact on patient's quality of life.

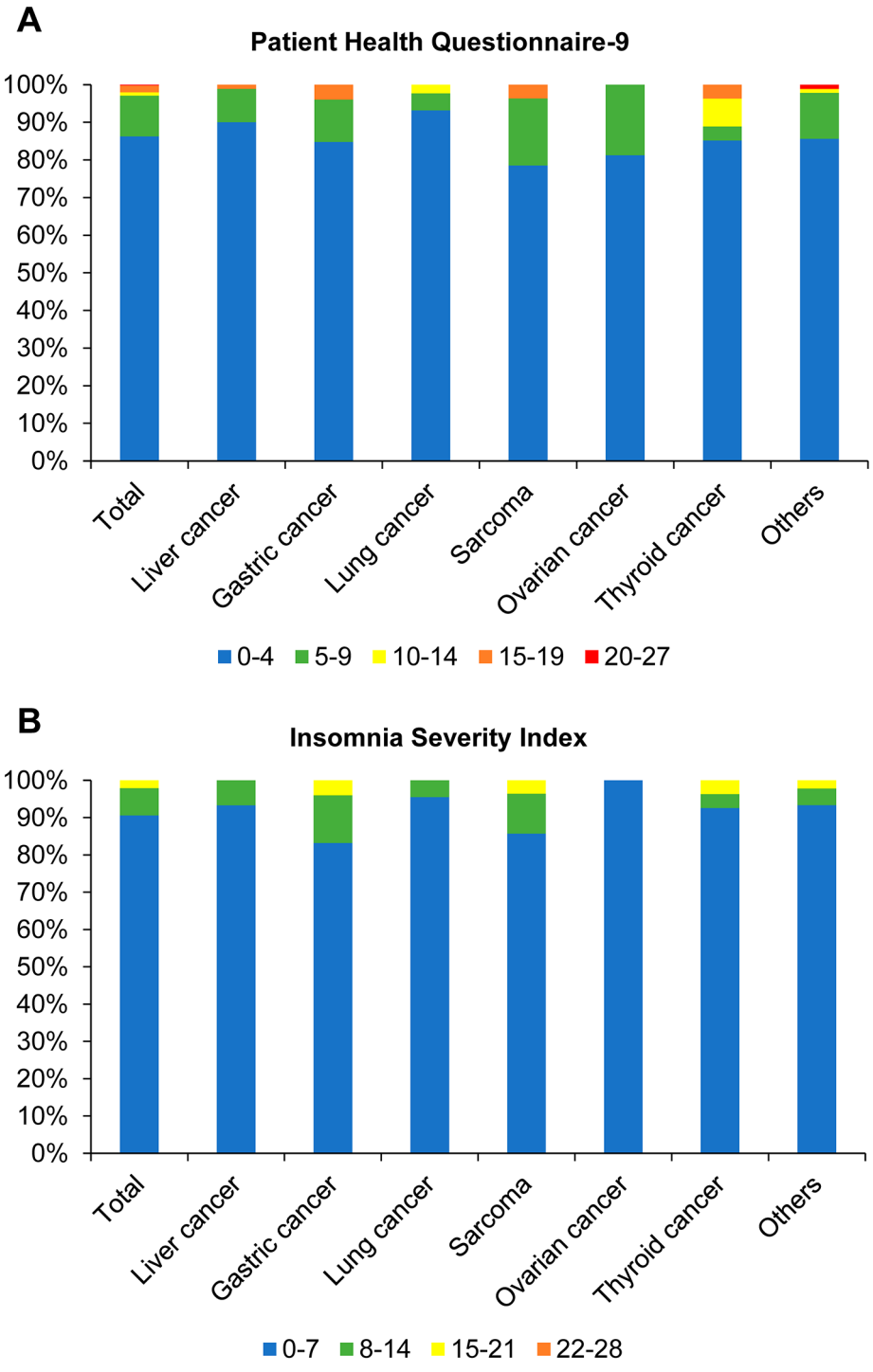

Fig. 1 Proportion of patients with different scores of Patient Health Questionnaire-9 (**A**) and Insomnia Severity Index (**B**)

The AE profile of apatinib-based therapy was similar with previous reports of phase 3 trials, but with a lower incidence [11–16]. Considering that the AEs were collected from questionnaire rather than medical records, there might be missing reports due to recall bias. In addition, patients might not be able to perceive some AEs (such as hematological toxicities) due to absence of symptoms. Nevertheless, the overall safety of apatinib was acceptable, and most patients were satisfied with it.

There are some limitations in this study. First, it is difficult to collect detailed disease information through an online questionnaire, thus the data on patient

Table 4 Patient-reported adverse events

Event	Total (*n* = 436)	Liver cancer (*n* = 125)	Gastric cancer (*n* = 90)	Lung cancer (*n* = 44)	Sarcoma (*n* = 32)	Ovarian cancer (*n* = 28)	Thyroid cancer (*n* = 27)	Others (*n* = 90)
At least one adverse event	195 (44.7)	62 (49.6)	29 (32.2)	20 (45.5)	15 (46.9)	16 (57.1)	13 (48.1)	40 (44.4)
Hand-foot syndrome	93 (21.3)	34 (27.2)	15 (16.7)	7 (15.9)	10 (31.3)	6 (21.4)	5 (18.5)	16 (17.8)
Hypertension	80 (18.3)	26 (20.8)	8 (8.9)	8 (18.2)	4 (12.5)	10 (35.7)	7 (25.9)	17 (18.9)
Proteinuria	20 (4.6)	3 (2.4)	1 (1.1)	2 (4.5)	1 (3.1)	5 (17.9)	2 (7.4)	6 (6.7)
Diarrhea	15 (3.4)	5 (4.0)	1 (1.1)	2 (4.5)	0	1 (3.6)	2 (7.4)	4 (4.4)
Nausea	8 (1.8)	1 (0.8)	1 (1.1)	2 (4.5)	0	1 (3.6)	0	3 (3.3)
Skin reaction	6 (1.4)	3 (2.4)	1 (1.1)	1 (2.3)	0	0	0	1 (1.1)
Abnormal liver function	6 (1.4)	3 (2.4)	1 (1.1)	0	0	1 (3.6)	0	1 (1.1)
Fatigue	3 (0.7)	2 (1.6)	1 (1.1)	0	0	0	0	0
Oral ulcer	3 (0.7)	2 (1.6)	1 (1.1)	0	0	0	0	0
Hypesthesia	2 (0.5)	0	1 (1.1)	0	0	1 (3.6)	0	0
Gastrointestinal bleeding	2 (0.5)	0	0	0	0	0	0	2 (2.2)
Epistaxis	1 (0.2)	0	0	0	0	0	0	1 (1.1)
Constipation	1 (0.2)	1 (0.8)	0	0	0	0	0	0
Non-infectious gingivitis	1 (0.2)	0	0	1 (2.3)	0	0	0	0
Hypothyroidism	1 (0.2)	0	0	0	0	0	0	1 (1.1)
Vomiting	1 (0.2)	0	0	0	0	0	0	1 (1.1)
Loss of appetite	1 (0.2)	1 (0.8)	0	0	0	0	0	0
Headache	1 (0.2)	1 (0.8)	0	0	0	0	0	0
Alopecia	1 (0.2)	1 (0.8)	0	0	0	0	0	0
Dyspepsia	1 (0.2)	0	0	0	0	0	0	1 (1.1)
Gingival pain and swelling	1 (0.2)	0	0	0	1 (3.1)	0	0	0

Data are *n* (%)

characteristics were limited in our study. Second, there may be a bias that patients who are satisfied with apatinib treatment maybe more willing to fill our questionnaire. Third, the AEs were collected by self-report rather than from medical records, and the patient-reported AEs could not be graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events. Fourth, this survey was conducted in patients who still survived and had received apatinib for at least 5 years, which did not involve patients with short survival after apatinib-based therapy. The 5-year survival rate and the associated factors for long survival could not be analyzed. Finally, the severity of depression and insomnia was assessed only once. The results of PHQ-9 and ISI could only reflect the conditions at that time. Changes in PHQ-9 and ISI scores before and after apatinib-based therapy were unknown. Further investigations are warranted to analyze the associated factors for long survival and changes in quality of life among patients treated with apatinib.

Conclusions

In conclusion, our survey showed a high satisfaction degree with apatinib in long-term cancer survivors. Apatinib treatment for at least 5 years resulted in almost no long-term negative impact on patient's quality of life.

Abbreviations

AE Adverse event
ISI Insomnia Severity Index
PHQ-9 Patient Health Questionnaire-9

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Author contributions

JL contributed to the study conception and design. TZ, CM, WH, TX, YY, CT, LZ, XS, CZ, XD, KW, CC, XY, HX, LH, EJ, FX, XZ, SZ, WZ, XL, J Zhang, J Zheng, JX, BH and GZ contributed to the acquisition of data. TZ, CM and J Zhu contributed to the analysis and interpretation of data. TZ and CM drafted the manuscript. All authors reviewed the manuscript. JL supervised the study. All authors have approved the final version of manuscript for submission.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committee of the Peking University International Hospital and all other participating centers. Written informed consent was obtained from each patient before participating in this survey.

Consent for publication

Not applicable.

Competing interests

Jiexiang Zhu is an employee of Jiangsu Hengrui Pharmaceuticals Co., Ltd. The other authors declare that they have no competing interests.

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