

# Quality of end-of-life care of advanced cancer patients in mainland China—a retrospective cohort of 441 hospital-death in a public funded comprehensive hospital

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**Background:** Shenzhen is a rapidly growing city in China with a population of over 11 million. The Hong Kong University-Shenzhen Hospital (HKU-SZH) was established in 2012 as a new model of publicly funded health care in mainland China. The clinical oncology center of the HKU-SZH was launched in 2013 which pledged to provide integrated palliative care for advanced cancer patients. This study aims to retrospectively analyze the quality of end-of-life care amongst patients with advanced cancer during their last hospitalization in the HKU-SZH.

**Methods:** Consecutive patients with advanced solid cancer who passed away in the HKU-SZH from March 2013 to February 2016 were analyzed. Clinical information regarding cancer diagnosis, anticancer treatments, and the aggressiveness of the treatment during the last month of life was recorded. The discussions on the Do-Not-Resuscitate (DNR) order with family members were reviewed.

**Results:** From March 2013 to February 2016, 441 patients with advanced solid cancer passed away in the HKU-SZH. A minority of them (9.3%, 41/441) received cytotoxic chemotherapy in the last month of life. Younger patients had high odds of receiving chemotherapy in their last month of life (OR 2.6, P=0.006). Those who received chemotherapy in their last month of life showed a trend of higher odds of admission to the intensive care unit (OR 2.94, P=0.08). The vast majority of family members / care providers (92.3%, 407/441) consented to the DNR order suggested by oncologists. The rate of DNR acceptance in this cohort was higher than previous reports from mainland China. Within HKU-SZH, the rate was higher in the oncology center than in other departments (OR 5.1, P<0.001). The use of chemotherapy in the last month of life did not associated with the acceptance of DNR (OR 1.3, P=0.23).

**Conclusions:** The integrated oncology service of the new public hospital HKU-SZH achieved a satisfactory level of end-of-life care in patients with advanced cancer. Further studies are warranted to improve the early integration of palliative care service and to investigate the impact of palliative care on cost-effectiveness of oncology service.

**Keywords:** Advanced cancer; palliative care; end of life; chemotherapy; Do-Not-Resuscitate; Hong Kong University-Shenzhen Hospital

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#### Introduction

Palliative care is an approach to improve the quality of life for patients and their care-givers facing problems associated with life-threatening illnesses (1,2). A growing body of evidence showed that integration of palliative care into standard oncology care resulted in improvements in quality of life, symptom control, patient and caregiver satisfaction, understanding of illness, quality of end-of-life (EOL) care, survival, and cost of care (3-5).

EOL care is an essential component of palliative care. There are various ways to assess the quality of end-of-life care service. The common indicators used to define overly aggressive palliative care in end-of-life services include (6): new anti-cancer therapies or continuation of treatments very near to death; excessive/unnecessary hospital admissions of advanced cancer patients in emergency rooms or intensive care unit (ICU); low utility of hospice services/ resources or late referral.

In mainland China, hospice services were in severe shortage (7). The majority of patients in cities tended to rely on case oncologists throughout their whole disease trajectory and were inclined to pass away in hospitals (8). Transferal of patients to a primary care unit or an organization with palliative care resources was often rejected by the patients and their families (9). Data of quality of end-of-life care services in various mainland cancer centers was still scarce.

Shenzhen city, a rapidly growing urban city in China with a population of approximately 11 million, shared similar problem with other major Chinese cities. In view of the huge shortage of oncology and palliative care service, the oncology center of the HKU-SZH was launched in 2013 which pledged to provide integrated oncology-palliative care service.

The HKU-SZH oncology center receives patient referrals from all other centers in China. Cancer patients might also be admitted to the center through emergency room of HKU-SZH. In the HKU-SZH oncology center, all advanced cancer patients were treated according to department's protocol for palliative care. The palliative care protocol outlined the multidisciplinary approach to tackle various aspects of symptom control, the use of strong opioid for pain control as well as psychosocial care of patients and their caregivers in distress. When patients approached the end-of-life period, the medical and nursing team of the center would initiate structured (EOL) care program in oncology ward.

In order to evaluate the effect of the palliative care program, the current study reviewed the EOL care quality indicators of HKU-SZH cancer center, which included the use of cytotoxic chemotherapy during the last month of life, admissions to the accident and emergency department (A&E) and ICU in the last month of life, and practice of Do-Not-Resuscitate (DNR) orders. We present the following article in accordance with the PRISMA reporting checklist (available at http://dx.doi.org/10.21037/apm-19-268).

#### **Methods**

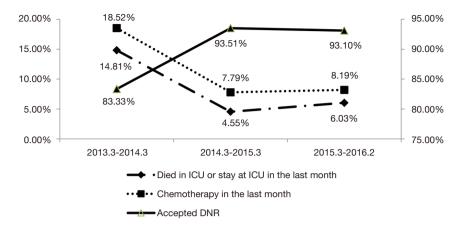
The study included all advanced solid cancer patients who expired at the HKU-SZH from March 2013 to February 2016. The clinical characteristics of patients recorded include, demographics, primary malignancy, date of recurrence or metastasis, death and last admission, last hospitalization through oncology clinics or accident & emergency department (A&E), lines of systemic anticancer therapies received, date of the last cycle of cytotoxic chemotherapy, initiation of new systemic anticancer therapies in the EOL period, the decision on DNR orders and the process leading to these, the use of cardiopulmonary resuscitation (CPR) and mechanical ventilation. The study had obtained the approval of HKU-SZH institutional review board (no: 2017-01).

Clinical descriptive data were presented as median and range. The relationships between each of the variables were assessed using the t test, chi-squared test, or Fisher's exact test. The Kaplan-Meier method was used for survival analysis. P<0.05 denoted statistical significance. The IBM@ SPSS@ 24.0 software was used for statistical analysis.

# **Results**

A total of 441 patients with advanced solid cancer expired in the HKU-SZH during the study period. The most prevalent primary malignancies were lung, liver & biliary, and colorectal cancer. The median age of patients was 62 years (range: 15–93 years). The average length of last hospitalization was 22.3 days (range: 1–302 days). About half (52.7%, 232/441) of the cohort was covered by the Shenzhen city medical insurance, in which 90% of the medical expenses were reimbursed. For the rest, 30–50% of the expenses were covered by basic medical insurance provided by other provinces which had lower rate of reimbursement.

The median overall survival of the cohort, counted



**Figure 1** The tendency for the administration of chemotherapy in the last month, acceptance to the DNR order, and admission to the ICU in the last month.

from the time of recurrence or metastasis to death, was 7 months (range: 0–83 months). Approximately half of the patients (47.2%; 207/441 patients) had never received any systemic anti-cancer treatment. In this group of patients, the commonest primaries were liver & biliary, lung, and stomach. The mean age of the group was older than the group who had received chemotherapy [mean age ± standard deviation (SD) 64.11±14.57; 57.16±13.94, P<0.001].

For chemotherapy use in the end-of-life period, 9.3% (41/441) underwent chemotherapy in the last month prior to death and 4.8% (21/441) in the last two weeks. Amongst those who underwent chemotherapy in the last month of their lives (41 patients), 68.3% (28/41 patients) received a new chemotherapy regimen. Patients with ovarian cancer received chemotherapy during the last month more frequently (33.3%; 7/21 patients) than patients with other types of cancer.

For the hospitalization data, more than half of the patients (51.5%; 217/441 patients) were admitted through the outpatient department, while 48.5% (214/441 patients) through the A&E. In the latter group, 46.7% (100/214 patients) visited the HKU-SZH for the first time and subsequently expired during this last hospitalization. Notably, 5.2% patients (23/441) expired in the ICU; 1.4% (6/441) were transferred to the ICU during the last month but afterwards expired in the general ward. CPR had been performed in 8.4% of patients (37/441), most frequently in the ICU (34.8%; 8/23 patients) compared with the wards of clinical oncology department (5.0%, 18/359) or other departments (18.6%, 11/59). These differences were

statistically significant (P=0.000).

Vast majority of patients (92.3%; 407/441) had DNR order in place before death. Within the group, 99.3% of the DNR order (404/407) were placed after discussion with family members but not with the patients themselves. The rate of DNR acceptance was higher in the clinical oncology center than other departments (OR 5.1, P<0.001). Despite the DNR order, 1.7% (7/407) patients still received CPR due to absence of family members when the patient was going to die.

The median time between the date of last admission to the placement of DNR was 9 days (range 0–131 days). The median time of the placement of DNR order before death was 2 days (0–89 days). The interval between DNR placement and death was not significant different for oncology center, ICU and other departments (P=0.13).

The tendency for the administration of chemotherapy in the last month, consent to the DNR order, and admission to the ICU in the last month are shown in *Figure 1*. Clinical characteristics in relation to the administration of chemotherapy in the last month and consent to the DNR order are presented in *Table 1*. There was no correlation between the two factors (OR 1.3, P=0.23).

## **Discussion**

The current cohort of consecutive 441 deceased patients with advanced cancer showed that satisfactory EOL care can be achieved with multidisciplinary, integrative palliative care services in an urban oncology center of mainland China. The overuse of chemotherapy and over-aggressive

Table 1 Clinical characteristics of patients in relation to the administration of chemotherapy in the last month and consent to the DNR order

Group	N	Chemotherapy in the last month		2	Р	Consent to the DNR order		- v <sup>2</sup>	Б
		No	Yes	- χ²	Ρ.	No	Yes	- χ <sup>2</sup>	Р
Gender				0.159	0.690			0.98	0.367
Male	256	231 (90.2%)	25 (9.8%)			17 (6.6%)	239 (93.4%)		
Female	185	169 (91.4%)	16 (8.6%)			17 (9.2%)	168 (90.8%)		
Age				7.519	0.006			1.923	0.211
≤62 years	222	193 (86.9%)	29 (13.1%)			21 (9.5%)	201 (90.5%)		
>62 years	219	207 (94.5%)	12 (5.5%)			13 (5.9%)	206 (94.1%)		
Location of death				8.353 <sup>a</sup>	0.015			55.76	0.000
Cancer center	359	324 (90.3%)	35 (9.7%)			14 (3.9%)	345 (96.1%)		
ICU	23	18 (78.3%)	5 (21.7%)			10 (43.5%)	13 (56.5%)		
Others	59	58 (98.3%)	1 (1.7%)			10 (16.9%)	49 (83.1%)		
Cancer primaries									
Head & neck	24	22 (91.7%)	2 (8.3%)			3 (12.5%)	21 (87.5%)		
Lung	120	108 (90.0%)	12 (10.0%)			5 (4.2%)	115 (95.8%)		
Esophagus & stomach	58	49 (84.5%)	9 (15.5%)			4 (6.9%)	54 (93.1%)		
Liver & biliary	65	64 (98.5%)	1 (1.5%)			7 (10.8%)	58 (89.2%)		
Colon-rectum	51	49 (96.1%)	2 (3.9%)			5 (9.8%)	46 (90.2%)		
Breast	19	17 (89.5%)	2 (10.5%)			1 (5.3%)	18 (94.7%)		
Cervix & corpus	15	13 (86.7%)	2 (13.3%)			3 (20.0%)	12 (80.0%)		
Ovary	21	14 (66.7%)	7 (33.3%)			0 (0.0%)	21 (100.0%)		
Pancreas	21	19 (90.5%)	2 (9.5%)			2 (9.5%)	19 (90.5%)		
Urine system	22	22 (100.0%)	0 (0.0%)			2 (9.1%)	20 (90.9%)		
Others	26	24 (92.3%)	2 (7.7%)			2 (7.6%)	24 (92.3%)		
Lines of therapy				11.53	0.003			2.41 <sup>a</sup>	0.30
0	208	199 (95.7%)	9 (4.3%)			20 (9.6%)	188 (90.4%)		
1–2	182	157 (86.3%)	25 (13.7%)			12 (6.6%)	170 (93.4%)		
≥3	51	44 (86.3%)	7 (13.7%)			2 (3.9%)	49 (96.1%)		
Median survival (months)		7	7			6	7		

<sup>&</sup>lt;sup>a</sup>Fisher's exact test.

EOL care (mechanical ventilation / ICU admission) in the last month of life were low at 9.3% and 9.2% respectively, and the placement of DNR order was achieved in 92.3% of all patients.

# The use of chemotherapy in the end-of-life period

The overuse of chemotherapy in the end-of-life period is

a common problem world-wide. It had been shown in a prospective study that the administration of chemotherapy in patients with end-stage cancer and a physician-estimated life expectancy of  $\leq 6$  months did not improve quality of life. Overuse of chemotherapy may be harmful even in patients with a good performance status (10).

The American Society for Clinical Oncology (ASCO) stated that discontinuation of EOL chemotherapy may

improve patient care and reduce cost (11). The ASCO recommended not to use cancer-directed therapy in patients with solid tumors who have the following characteristics: poor performance status (3 or 4), no benefit from prior evidence-based interventions, ineligibility for a clinical trial, and weak evidence supporting the clinical value of further anticancer treatment.

However, according to a survey from African cancer center (12), among all adult patients with reported cancer deaths between 2014 and 2015, 65.9% received chemotherapy and more than 45% of patients received chemotherapy in the last 30 days of life. In France (13), among a total of 279,846 hospitalized patients who died from metastatic cancer between January 2010 and December 2013, there were 19.5% of patients received chemotherapy during the last month before death, and 11.3% during the last 2 weeks. Compared with university hospitals, patients who died in profit-making clinics/hospital or comprehensive cancer centers were more likely to receive chemotherapy. High-volume centers and hospitals without palliative care units reported greater-than-average rates of chemotherapy near the end of life. A retrospective study investigating 3,350 decedents from six representative hospitals across China from 2010 through 2014 reported that 16.9% of patients received chemotherapy during the last month of their lives (14).

The phenomenon of over-using chemotherapy might be attributed to a number of reasons. Firstly, oncologists often fail to accurately estimate the survival of individual patients (15). Over-optimistic estimation may lead to continual use of late-line chemotherapy. Secondly, a number of patients did not recognize that chemotherapy was not going to cure their cancer (16). Patients with an understanding of the incurable nature of cancer were less likely to receive chemotherapy in EOL period and associated with increased enrollment to hospice services prior to death (17).

In the present study at the HKU-SZH, 9.3% of patients received cytotoxic chemotherapy during the last month. This percentage was relatively low compared with other reports in the literature as listed above. For example, one major hospital in Central China reported more than 40% chemotherapy use in the last 1-3 months of life (18). This favorable outcome may be attributed to several reasons.

Firstly, in the HKU-SZH, we emphasized open and thorough communication of the treatment plan with families (19). In the communication process, we discussed the prognosis and defined the goal of care. We actively offered the option of best supportive care alone among the

patients who had very poor prognosis and no evidence-based anti-cancer treatment options. Besides, if the patients and families decided to try a new chemotherapy regimen with limited evidence or efficacy, such decisions would be reviewed by senior oncologists. Once late-line chemotherapy was initiated, patient would be closely monitored for the treatment response and toxicity. The team would promptly stop the treatment if the early results of the regimen was unfavorable.

Another notable finding was that 47.2% of patients in the current cohort had never received cytotoxic chemotherapy or other systemic anti-cancer therapies. This group of patients were older, and more likely to have primaries of lung, hepatobiliary tract and stomach. Possible reasons for this phenomenon were manifold. It might be related to the lack of effective systemic treatment options for these cancers. This was especially the case before the approval of immunotherapies in China. Many novel targeted agents, which might be less toxic than conventional chemotherapy, were either not available or too expensive in mainland China at the time of the cohort. Besides, integrated palliative care was readily provided by the HKU-SZH team which was a reasonable alternative to the ineffective and toxic systemic treatments.

The present study identified that younger patients and patients who had undergone previous anticancer therapies are more likely to continue chemotherapy in the last month of their life. Furthermore, our data suggest that patients with ovarian cancer are most likely to receive chemotherapy in the last month. These results were consistent with other reports (20). Further studies are needed to evaluate the decision-making process as well as the impact of such an aggressive approach on EOL care and bereavement process of care-givers.

# Emergency admission and ICU utilization in the EOL period

The present study found that 48.5% of patients with advanced cancer were admitted via the A&E department. In this group of patients, about half of them were visiting HKU-SZH for the first time and subsequently expired during the admission.

The cause of such high rate of A&E utilization was multifold. The home-care service or family physician system were in infancy in mainland China. The social support of patients at Shenzhen City was also weaker than traditional community as Shenzhen is a city of immigrants. Many

patients were thousand miles away from their ancestral home and hence was inaccessible to their social supportive network.

Besides, many hospitals in the city were reluctant to admit critically ill late-stage cancer patients while HKU-SZH A&E had performance pledge to accept all patients. The high rate of A&E utilization was consistent with other reports, including the study conducted at the Seoul National University Hospital that (21) visits to the emergency room by cancer patients during the last month of their life had increased from 22.8% in 2002 to 74.8% in 2012.

For ICU utilization in EOL period, the rate improved from 18% in the first year of HKU-SZH service to 4–5% in 2<sup>nd</sup> to 3<sup>rd</sup> year. The rate was comparative low compared with other major center in mainland China which reported the rate of around 25% (18). The improvement was likely contributed to maturation of the clinical teams and improved collaboration amongst different departments. In the current cohort, the use of chemotherapy in the last month was strongly associated with ICU admission in the EOL period. This was consistent with other reports which suggested chemo in EOL period was associated with an increased risk of undergoing CPR, mechanical ventilation, and dying in the ICU (22,23).

# Placement of DNR orders

In the present study at the HKU-SZH, the overall rate of consent to the DNR order was >90%. In a similar report at Guangdong Lung Cancer Institute, Wang *et al.* reported that consent to the DNR order among patients with lung cancer was 74.7% (24). This disparity may be due to different practices between these two medical institutions. The Guangdong Lung Cancer Institute is a specialized lung cancer center focusing on the anticancer treatment. In contrast, the HKU-SZH Cancer Center is a general comprehensive hospital aiming at provision of integrated palliative care service.

The current cohort at Shenzhen and another palliative care unit from Shanghai report (25) were different from Western reports that most of the DNR order was placed after discussion of health care team with the families, rather than patients themselves. The median interval between the placement of DNR order and death was 2 days, that means most of the DNR decision occurred very close to patients' death. Such a "last minutes" DNR order was common in mainland China. This was probably related to the cultural meaning of "seeing the patient for the last time". Doctors

usually would not consider DNR until the impending death was certain and would wait until all the significant family members had "seen" the patients.

The rate of DNR placement differed between departments with HKU-SZH, being higher in the clinical oncology center (96.1%) than other departments (83.1%). The team approach of clinical oncology center may contribute to this higher success rate of DNR placement. This highlighted the importance of integrative palliative care team in acute hospital setting and the need of more training on EOL care in other clinical departments.

#### Limitations

The major limitation to our study was that the data were retrospectively collected in design. Besides we could not review the minority of patients (n<10) who were discharged near death, which might have affected the accuracy of the rate of chemotherapy in the last 30 days. We are conducting a prospective longitudinal observational study in a cohort of patients with advanced cancer admitted in the palliative unit in HKU-SZH. We are also in the process of standardizing an integrative palliative care model reimbursement system of Shenzhen.

#### **Conclusions**

The integrative oncology service of the new public hospital HKU-SZH had yielded a satisfactory level of palliative care in advanced cancer patients. Further studies are warranted to investigate the impact of the system on quality of life of patients and their caregivers, as well as the best model to promote early integration of palliative care in mainland China.

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#### Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study had obtained the approval of HKU-SZH institutional review board (no: 2017-01). As it is a retrospective descriptive study, there was no informed consent.

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