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Research article

Impact of infection on healthcare costs and clinical outcomes in elderly hospitalized patients with multimorbidity

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ABSTRACT

Background: Elderly patients with multimorbidity are at higher risk of greater healthcare costs and poor outcomes due to decreased physical function. The aim of this study was to investigate the impact of infection on healthcare costs and poor outcomes in elderly hospitalized patients with multimorbidity.

Methods: We retrospectively enrolled 264 patients who met the inclusion criteria from the department of geriatrics of a large public hospital in Shanghai, China between January 2020 and December 2020. Patients were divided into two groups based on whether they had infection [infection present on admission (IPOA) or healthcare-associated infection(HAI)]. We recorded the basic information and follow-up information of all patients. The follow-up information included 30-day and 1-year all-cause readmission and mortality. Then we analyzed the association between infection and healthcare costs and clinical outcomes.

Results: Among 264 subjects, 47.73 % of them achieved IPOA or HAI. The 30-day poor outcomes rate was 45.45 %, and the 1-year poor outcomes rate was 78.41 %. Compared with subjects without infection, the number of drugs and the disease burden were greater in subjects with infection($P < 0.001$). Subjects with infection had longer length of hospital stay($P < 0.001$) and had greater healthcare cost($P < 0.001$). Moreover, subjects with infection had higher poor outcomes rates of 30-day and 1-year($P < 0.001$). Infection could predict greater total cost [odds ratio (OR): 1.32, 95 % CI: 1.18,1.49,$P < 0.001$], nursing cost(OR: 11.45, 95 % CI: 3.49,37.63,$P < 0.001$), and medicine cost (OR: 2.37, 95 % CI: 1.70,3.31,$P < 0.001$). In addition, infection was also independently associated with the 30-day poor outcomes rate(OR:3.07, 95%CI: 1.80,5.24,$P < 0.001$), but we found no association between infection and 1-year poor outcomes rate(OR:1.43, 95 % CI:0.73,2.79,$P = 0.300$) after adjustment.

Conclusions: Infection was a risk factor for higher healthcare cost and 30-day poor outcome rate in elderly hospitalized patients with multimorbidity.

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1. Introduction

China is facing severe healthcare challenges from its large aging population. It is predicted that people over 65 years old in China will reach 400 million by 2050 [1]. Aging has increased the number of elderly hospitalized patients, especially those with multimorbidity [2–4]. These patients often suffer from high risk of poor outcomes such as readmission and mortality, which will lead to high healthcare cost, and place a heavy burden on health care resources [3,5]. As a result, efforts to investigate the risk factors of high healthcare costs and poor outcomes for elderly hospitalized patients with multimorbidity have received significant attention.

Elderly people with multimorbidity face more risks and challenges than those without chronic diseases. They have more than four times the risk of developing activities of daily living (ADL) disability [6], and the risk of high healthcare costs and poor outcomes are higher than that of other inpatients [5,7]. A study of elderly community population found patients with multimorbidity were 5.6 times more likely to be hospitalized, and the total healthcare costs per year were 5.5 times higher in patients with multimorbidity [6]. So it is necessary to explore the factors influencing healthcare costs and poor outcomes in elderly patients with multimorbidity. But studies are still scarce in terms of the impact of influencing factors.

Infection which occurs in hospitalized patients is an apparent public health concern. Previous studies have proven that infection could increase the risk of poor outcomes and healthcare costs [8,9]. Both infection present on admission (IPOA) and healthcare-associated infection (HAI) are associated with mortality and readmissions [10]. Meanwhile, they also represent a significant economic burden for health care systems in many countries [9,11]. However, there is limited evidence reporting the impact of infection on healthcare costs and clinical outcomes in elderly hospitalized patients with multimorbidity.

Therefore, the aim of this study was to investigate the impact of infection on healthcare costs (total cost, nursing cost, and medical cost) and poor outcomes (the mortality and readmission rate of 30-day and 1-year after discharge) rate in elderly hospitalized patients with multimorbidity.

2. Materials and methods

2.1. Study design and participants

This was a retrospective, cross-sectional study of elderly inpatients with multimorbidity. Participants were recruited consecutively between January 2020 and December 2020 from the department of geriatrics of Shanghai East Hospital, Tongji University School of Medicine, Shanghai, China. Inclusion criteria: 1) $\geq$60 years old; 2) diagnosed with multimorbidity [12] (presence of at least two chronic diseases according to the International Classification of Diseases, 11th Revision (ICD-11)); 3)length of hospital stay$\geq$3 days; 4) informed consent. Exclusion criteria: 1) patients who were admitted with non-multimorbidity factors (such as acute trauma); 2) patients whose medical records lacked important data; 3) patients who were lost to follow-up.

Infection included IPOA and HAI. IPOA was considered infection that occurs within 48 h of admission. HAI was considered to be infection during hospitalization and there must be no evidence of an infection at admission [10]. The variables selected for this study were based on factors showing an effect on both healthcare costs and outcomes in the previous studies [13]. We recorded the basic information (age, sex, disease history, healthcare costs information and drug information) of all patients. The follow-up information of this study were outcomes of 30-day and 1-year after discharge, defined as all-cause readmission or mortality. Cumulative Illness Rating Scale (CIRS) [14] is among the most valid and reliable measures of multimorbidity. It has good inter-and intra-rater reliability. The CIRS has been reported to be a valid indicator of health status in geriatric patients, and also to be able to predict outcomes for elderly patients [15]. The CIRS scoring and outcome assessment were performed by two trained physicians blinded to other information with a structured follow-up telephone interview with the patients or, if not possible, with their family members. This study was approved by the Ethics Committee of Shanghai East Hospital, Tongji University School of Medicine (NO. [2022] 117).

2.2. Disease burden

We firstly assessed the total number of chronic conditions and prescribed drugs during the hospitalization. Then the severity of each condition was graded by CIRS which ranged from 0 to 4: 0 = normal organ function, 1 = mild discomfort, symptoms or disability, easy to control, 2 = moderate discomfort, symptoms or disability, manageable, 3 = severe discomfort, symptoms or disability, hard to control, and 4 = life threatening, permanently disabling disability, causing organ failure, poorly manageable. Finally, we took the sum of the severities of all chronic conditions as disease burden.

2.3. Healthcare costs

The information of healthcare cost included nursing care cost, medicine cost and other cost (such as the cost of laboratory diagnosis, pathological diagnosis, imaging diagnosis, rehabilitation, and disposable medical materials for examination), with the medicine cost and nursing care cost accounting for the highest proportion, so we recorded the nursing care cost, medicine cost, and total cost from the home page of medical records.

3. Clinical outcomes

The clinical outcomes include mortality and readmission. Mortality was considered all-cause death in-hospital and after discharge.

The latter was assessed at 30 days and 1 year after discharge, by telephone interview with patients or their family members. Readmission was defined as all-cause readmission. For each admission, readmissions were identified within 30 days and 1 year of discharge. If multiple readmissions occurred, only the first was evaluated to prevent double counting.

3.1. Statistical analysis

We performed statistical analysis using SPSS22.0 software (IBM SPSS, Armonk, NY, USA). Patients were divided into two groups based on whether they had infection. The categorical variables were expressed as number and percentage and analyzed with the chi-square test. Continuous variables which exhibit normally distributed data were expressed as mean and SD, otherwise as median and interquartile range, and analyzed with the Mann–Whitney *U* test or Student's t-test. Univariate and multivariate logistic regression analysis was used for investigating the impact of infections on healthcare costs and clinical outcomes. Variables with $P < 0.1$ in univariate analysis were included in the multivariate logistic regression analysis. $P < 0.05$ was considered to be statistically significant.

4. Results

4.1. Patient characteristics

A total of 264 subjects who met the inclusion criteria were ultimately enrolled in this study, and the rate of lost to follow-up was 5.7 % (16/280). The median age was 89 (85,91) years old, and 76.13 % (n = 201) were male, 47.73 % (n = 126, IPOA = 47, HAI = 79) of them achieved infection. The median number of diseases was 7(6,9), the median number of drugs was 14(10,17), the median disease burden was 14(12,17), and the median length of hospital stay was 27(12,40.75) days (Table 1).

The median total cost was 4.94(4.07,5.80) thousand dollars, the median nursing cost was 0.35(0.30,0.41)thousand dollars, and the median medicine cost was 2.08(1.61,2.55) thousand dollars (Table 2). The 30-day poor outcomes rate was 45.45 %, and the 1-year poor outcomes rate was 78.41 % (Table 2).

4.2. Comparison between subjects with infection and without infection

There was no difference in age, sex, and the number of disease between two groups($P > 0.05$). Compared with subjects without infection, the number of drugs and the disease burden were greater in subjects with infection ($P < 0.001$) (Table 1). We also found that subjects with infection had a longer length of hospital stay($P < 0.001$) and higher healthcare costs ($P < 0.001$). Moreover, subjects with infection had higher poor outcomes rates of 30-day and 1-year after discharge($P < 0.001$) (Table 2).

4.3. Logistic regression analysis

We performed logistic regression analysis to assess whether infection was independently associated with healthcare costs and poor outcomes (readmission or mortality) after adjustment by clinical variables [age, number of drugs and disease burden with $P < 0.1$ in univariate analysis (Table 3)]. We found infection could predict greater total cost[odds ratio (OR): 1.32, 95 % CI: 1.18,1.49, $P < 0.001$], nursing cost(OR: 11.45, 95 % CI: 3.49,37.63, $P < 0.001$), and medicine cost (OR: 2.37, 95 % CI: 1.70,3.31, $P < 0.001$). In addition, infection was also independently associated with the 30-day poor outcomes rate(OR: 3.07, 95 % CI: 1.80,5.24, $P < 0.001$), but we found no association between infection and 1-year poor outcomes rate(OR: 1.43, 95 % CI: 0.73,2.79, $P = 0.300$) after adjustment(Table 4). Moreover, in subgroup analyses we found that IPOA was not associated with higher costs and poor outcomes, but HAI was significantly associated with higher costs and 30-day poor outcomes (Table 5).

5. Discussion

Healthcare costs and clinical outcomes are important for hospitalized patients. We investigated the influence of infection (IPOA and HAI) on healthcare costs and clinical outcomes in elderly hospitalized patients with multimorbidity and found infection was

Table 1
Baseline characteristics of subjects.

	Total(n = 264)	Infection(n = 126)	Non-infection(n = 138)	P value
Age(yeas)				0.060
60≥age<70	64.50(62.75,68.25)	65.50(62.75,68.25)	64(62.75,68.25)	
70≥age<80	77.50(73.00,79.00)	77.50(71.00,79.00)	77.50(73.25,79.00)	
80≥age	90.00(87.00,91.00)	90.00(88.00,91.00)	89.00(87.00,91.75)	
Male (%)	201(76.14 %)	95(75.40 %)	106(76.81 %)	0.885
Number of diseases	7(6.00,9.00)	7(6.00,9.00)	7(6.00,9.00)	0.261
Number of drugs	14(10.00,17.00)	15.5(13.00,20.00)	12(9.00,15.00)	<0.001[a]
Disease Burden	14(12.00,17.00)	16(12.75,18.25)	13(10.00,16.00)	<0.001[a]
Length of hospital stay(days)	27(12.00,40.75)	31.5(17.00,80.75)	18.5(10.00,30.25)	< 0.001[a]

[a] $P < 0.05$.

Table 2
Healthcare costs and clinical outcomes information of subjects.

	Total(n = 264)	Infection(n = 126)	Non-infection(n = 138)	P value
Total cost (thousand dollars)	4.94(4.07,5.80)	7.48(5.79,9.16)	2.62(2.29,2.94)	<0.001[a]
Nursing cost (thousand dollars)	0.35(0.30,0.41)	0.49(0.39,0.58)	0.23(0.20,0.27)	<0.001[a]
Medicine cost (thousand dollars)	2.08(1.61,2.55)	3.52(2.60,4.44)	0.76(0.64,0.88)	<0.001[a]
30-day bad clinical outcome rate (%)	120(45.45 %)	76(60.32 %)	44(31.88 %)	<0.001[a]
1-year bad clinical outcome rate (%)	207(78.41 %)	107(84.92 %)	100(72.46 %)	0.016[a]

[a] $P < 0.05$.

Table 3
Univariate logistic regression analysis of the impact of infection on basic characteristics.

	OR (95%CI)	P value
Age	1.04(1.01,1.07)	0.039[a]
Male	1.08(0.61,1.90)	0.788
Number of diseases	1.06(0.97,1.07)	0.196
Number of drugs	1.15(1.09,1.21)	<0.001[a]
Disease Burden	1.14(1.07,1.20)	<0.001[a]
Length of hospital stay	1.01(0.99,1.02)	0.495

OR, Odd Ratio; CI, Confidence Interval.
[a] $P < 0.05$.

Table 4
Univariate and multivariate logistic regression analysis of the impact of infection on healthcare costs and clinical outcomes.

	Univariate logistic regression		Multivariate logistic regression	
	OR (95%CI)	P value	OR (95%CI)	P value
Total cost (thousand dollars)	1.38(1.24,1.54)	<0.001[a]	1.32(1.18,1.49)	<0.001[a]
Nursing cost (thousand dollars)	15.71(5.55,44.47)	<0.001[a]	11.45(3.49,37.63)	<0.001[a]
Medicine cost (thousand dollars)	2.43(1.81,3.25)	<0.001[a]	2.37(1.70,3.31)	<0.001[a]
30-day bad clinical outcome rate (%)	3.25(1.96,5.38)	<0.001[a]	3.07(1.80,5.24)	<0.001[a]
1-year bad clinical outcome rate (%)	2.14(1.16,3.96)	0.015[a]	1.43(0.73,2.79)	0.300

OR, Odd Ratio; CI, Confidence Interval.
[a] $P < 0.05$.

Table 5
Univariate and multivariate logistic regression analysis of the impact of HAI on healthcare costs and clinical outcomes.

	Univariate logistic regression		Multivariate logistic regression	
	OR (95%CI)	P value	OR (95%CI)	P value
Total cost (thousand dollars)	1.14(1.07,1.21)	<0.001[a]	1.11(1.03,1.19)	0.004[a]
Nursing cost (thousand dollars)	4.23(1.83,9.80)	0.001[a]	2.54(1.03,6.28)	0.043[a]
Medicine cost (thousand dollars)	1.38(1.19,1.59)	<0.001[a]	1.31(1.12,1.54)	0.001[a]
30-day bad clinical outcome rate (%)	2.874(1.66,4.96)	<0.001[a]	2.72(1.52,4.86)	0.001[a]
1-year bad clinical outcome rate (%)	2.37(1.13,4.97)	0.001[a]	1.66(0.76,3.65)	0.205

OR, Odd Ratio; CI, Confidence Interval.
[a] $P < 0.05$.

independently associated with the healthcare costs and 30-day poor outcomes in elderly patients with multimorbidity.

To our best knowledge, this was the first study to report the impact of infection on the healthcare costs and clinical outcomes in hospitalized elderly patients with multimorbidity. Addressing the healthcare costs is essential if a country is to remain economically competitive globally. An uncontrolled increase in health care cost will not only affect the ability to provide quality care to patients, but also threaten the ability of the country to compete economically [16]. We found infection could increase healthcare costs. This association was still significant after adjusting age, number of drugs and disease burden. Previous studies of other countries reported similar findings [17,18]. A retrospective cohort study conducted in Thailand found infection was significantly related with higher hospitalization costs [19]. A meta-analysis study showed that the total costs for the 5 major infections were $9.8 billion per year in US [17]. Shelanah A Fernando reported Australia spent more than $1 billion on HAI annually. Moreover, patients and communities would suffer significant and unmeasured physical, psychological and economic costs [18].

The 30-day poor outcomes rate and 1-year poor outcomes rate of infection subjects were higher than those without infection. But only the 30-day poor outcomes rate was independently associated with infection after adjustment. Many researches have reported the

similar results of 30-day poor outcomes [20–22]. But a previous study found that about 35 % of HAI patients were readmitted to hospital within 1 year after discharge [23]. Carley B. Emerson, MS et al. reported patients with infection might be at increased risk of hospital readmission within 1-year after discharge [24]. The differences might be related the larger fraction of older and multimorbidity subjects in this study, age and multimorbidity were associated with the 1-year readmission rate [25], and no studies have compared the magnitude of the effects of multiple diseases and infection on poor outcomes rates. In addition, the infection in this study included IPOA and HAI which was different from many other studies.

Multimorbidity and polypharmacy may lead to conflicting specialist advice and lack of coordination in the clinical and therapeutic management of the patient, which can expose older patients at higher risk of HAI [26].The subgroup analyses of this study showed that only HAI was significantly associated with higher costs and 30-day poor outcomes. Another study revealed that HAI was an independent risk factor for admission to the ICU and hospital mortality in patients over 85 years of age [27]. Immunosenescence is present in all older adults to varying degrees, the normal capabilities of defense against infection declines [28]. Many older adults have mild degrees of immunosuppression as a result of immunosenescence, together with age related organ changes, comorbidities, geriatric syndromes, frailty, malnutrition, functional dysfunction and, polypharmacy, all of which affect the outcomes of elderly patients with HAI. Therefore, it is important to take necessary measures to prevent HAI in hospitalized elderly people [29].

In this study, we found that IPOA was not associated with healthcare cost and clinical outcomes. But this was inconsistent with previous findings. Gonçalves-Pereira J et al. reported infection, regardless of its place of acquisition, was associated with increased mortality of patients admitted to the Intensive Care Unit [30]. Other studies reported severe community-acquired pneumonia patients had worse outcomes [31,32]. The differences in the findings may be related to the different populations included in the studies. The elderly population has more factors affecting their healthcare costs and outcomes due to the decline in body functions. This might make a difference in the extent to which IPOA affects the healthcare costs and outcomes of elderly patients. Therefore, a study with a larger sample size is needed to investigate the extent to which each factor affects the healthcare costs and outcomes of elderly patients.

Besides, we found a relatively high incidence (47.73 %) of infection compared with previous studies [19]. This might be related to the older age of the subjects in this study, and the incidence of HAI was higher in older people [33]. Moreover, some studies only included the rate of IPOA or HAI, but we included the rate of both IPOA and HAI. Although there was no significant difference in the number of diseases between patients with and without infection, the former had a higher drug number and heavier disease burden, and the differences were still statistically significant in logistic regression analysis. Similar results were reported by other researchers [34,35]. Andrea Ticinesi et al. found that multimorbidity, as measured by the CIRS Comorbidity Score, were independently associated with hospital-acquired Clostridium difficile infection risk in elderly hospitalized patients [36]. A longer length of hospital stay was found in the infection group, but there was no difference between two groups in logistic regression analysis. This was different from other researches [37,38]. This might be related to the fact that the subjects in this study were elderly, and there were more factors to prolong the length of hospital stay, which should be further verified by prospective large sample study.

This study has not only strengths but also limitations. First, this was a single center retrospective study with a relatively small sample size of 264 patients, this might lead to higher selection biases and limit the generalizability of the findings. So it is necessary to conduct a larger sample study to further validate the findings of this study. Second, we did not specify the site and cause of infection to further analyze the strength of the impact of different infections on healthcare costs and poor outcomes rates. But there might be differences in the extent to which infections in different systems affect outcomes and healthcare costs, which need to be further explored in future studies. Third, although infections were assessed by blood test, asymptomatic infections might have been missed. In addition, the healthcare costs classification method may vary from hospital to hospital and will need to be further refined if multicenter studies are conducted in the future.

6. Conclusions

In conclusion, our results suggested that infection was independently associated with a significantly higher healthcare costs and 30-day poor outcomes rate in elderly inpatients with multimorbidity. Preventing infection, especially preventing HAI, might be effective in reducing healthcare costs and poor outcomes rate in elderly inpatients with multimorbidity.

Ethical approval

This study was approved by the Ethics Committee of Shanghai East Hospital, Tongji University School of Medicine (NO. [2022] 117).

Informed consent

Each patient provided written informed consent.

Consent for publication

The manuscript has been approved by all authors for publication.

Data availability

The raw data supporting the conclusions of this manuscript will be made available by the authors, without undue reservation, to any qualified researcher.

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Authors' contributions

Hua Jiang designed the study. Xin Chen and Shasha Geng collected information, analyzed data, and wrote the article. Yingqian Zhu and Qingqing Li contributed to information collection, reviewed and revised the article before the submission. Yang Li and Huixiao Yuan contributed to information collection and data analysis.

Declaration of competing interest

We would like to submit this manuscript titled ***Impact of Infection on Healthcare Costs and Clinical Outcomes in Elderly Hospitalized Patients with Multimorbidity*** for possible publication in **Heliyon**. The authors of this manuscript declared that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

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Abbreviations

IPOA	infection present on admission
HAI	healthcare-associated infection
ICD-11	International Classification of Diseases, 11th Revision
CIRS	Cumulative Illness Rating Scale

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