
Report C

Traditional Chinese medicine in the management of patients with SARS in Hong Kong Special Administrative Region — a case–control study of 24 patients

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Abstract. Traditional Chinese medicine (TCM) is not the first-line treatment for severe acute respiratory syndrome (SARS) in Hong Kong Special Administrative Region (SAR). From May 2003, 48 inpatients received individualized TCM treatment, of whom 24 were successfully matched to 107 controls with comparable age, sex, comorbidities and disease severity. Relative to the matched controls, survivors of SARS who had received complementary TCM benefited by needing a shorter hospital stay (a reduction of 4 days, $p < 0.05$), requiring less steroid (6 g less, $p < 0.05$) and shorter duration of steroid treatment (2 days fewer, $p < 0.05$). The survival rate following interventional complementary TCM care (70% of patients received TCM treatment > 21 days after onset of symptoms), was not significantly different from that in matched controls. SARS patients who received TCM treatment benefited from improvements in symptoms including fatigue, dry mouth, dyspnoea and loose stools. Shortening of hospital stay was most marked in patients who first received TCM treatment < 28 days after onset of symptoms, suggesting that early provision of TCM care in SARS patients may be most beneficial for patients. The benefit of requiring less steroid treatment was observed in all patients treated with TCM regardless of when treatment started. Our results indicate that SARS patients treated with TCM benefited from shorter hospitalization, a substantial decrease in steroid administered, and improvement of symptoms.

Background

The public hospitals of Hong Kong SAR offer no TCM service on their wards. In May 2003, two TCM physicians who were experienced in the treatment of SARS in Guangzhou, China, were invited by the Hospital Authority of Hong Kong to provide complementary TCM care to SARS inpatients in public hospitals in Hong Kong SAR.

This report describes a study that aimed to compare the effects of complementary TCM on SARS patients with matched controls who received conventional (Western) medical care only.

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Methods

Design

A case-control study design was used.

Access to Traditional Chinese medicine

SARS patients in public hospitals of Hong Kong SAR were eligible for TCM care if the following three conditions were fulfilled.

1. Patients themselves requested TCM care.
2. Attending doctors (Western medicine) endorsed such requests.
3. TCM physicians considered that patients were suitable for TCM treatment.

In fact, condition 3 was never applied. All requests for TCM care that fulfilled conditions 1 and 2 above were granted.

Source of data

Demographic data and details of treatments received by the study subjects were extracted from a SARS-specific territory-wide database constructed by the Hospital Authority of Hong Kong SAR. TCM-related data (mostly in Chinese) were collected from the hospitals where the patients were being treated. The dates were processed in a separate database in Kwong Wah Hospital using patients' unique Hong Kong identity numbers for indexing.

Patient profiles

Forty-eight SARS patients received TCM care (Table 1). The ratio of females to males was 2:1 and the mean age was 45.1 years for males and 42.5 years for females. Eighty per cent of patients received TCM 14 days or more after admission (Fig. 1). Seventy per cent of patients first received TCM 21 days or more after onset of symptoms (Fig. 2). On average, patients first received TCM care 31.6 days after admission and 34.3 days after onset of symptoms.

Table 1. Demographic profiles of SARS patients who received treatment with traditional Chinese medicine

		Comorbidities?				Total	Percentage
		No		Yes			
		Survived	Died	Survived	Died	<i>n</i>	
Sex	Age (years)						
Female	21-40	11	3	-	-	14	29.2
	41-60	10	2	2	3	17	35.4
	61-80	-	2	-	1	3	6.3
Male	21-40	3	2	-	-	5	10.4
	41-60	4	2	-	1	7	14.6
	61-80	1	-	1	-	2	4.2
All		29	11	3	5	48	100.0

Fig. 1. Number of days between starting TCM treatment and admission to hospital

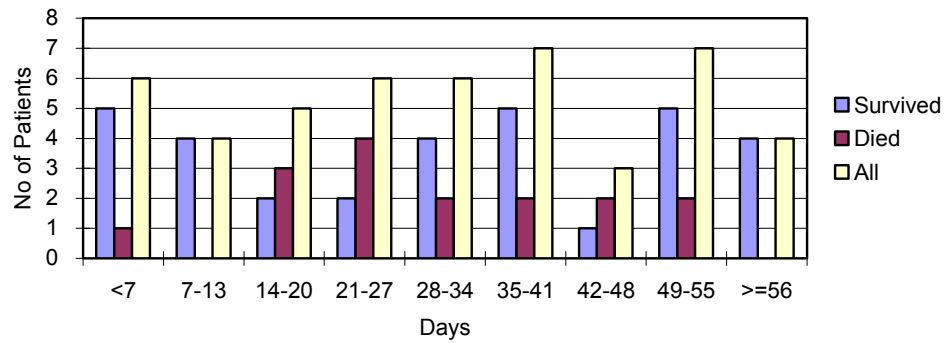


Fig. 2. Number of days between starting TCM treatment and onset of symptoms

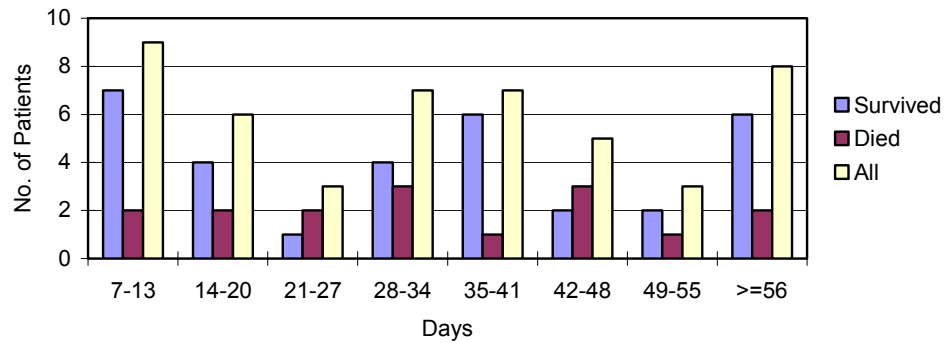
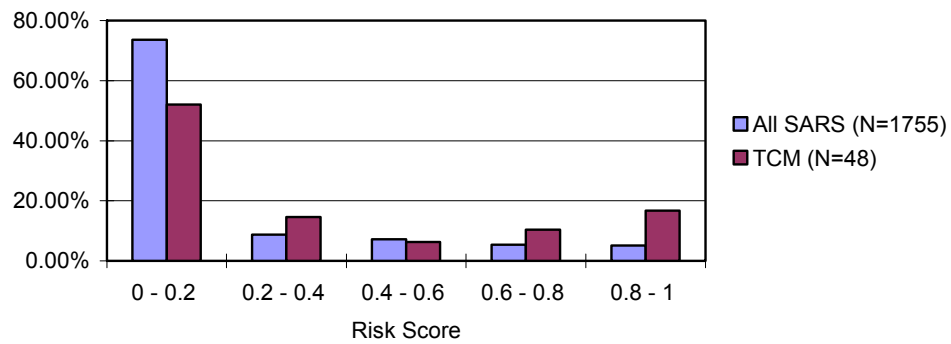


Fig. 3. Risk score distribution for SARS patients at start of treatment with traditional Chinese medicine



Risk profiles of patients

Based on gender, age, presence of comorbidities (including chronic obstructive airway disease, ischaemic heart disease, cerebrovascular disease, cancer, diabetes and chronic liver disease), serum lactate dehydrogenase (LDH) levels and respiratory status on admission (1, 2), we used multivariate logistic regression on risk scores equivalent to the probability of death for all SARS patients (Fig. 3). Patients who received TCM care represented a subset that had higher risk scores at the time when they first received TCM.

A risk score (equivalent to probability of death) was calculated by logistic regression using five prognostic factors (age, sex, comorbidity, lactate dehydrogenase and respiratory status) of 1755 SARS patients from Hong Kong SAR at the start of treatment.

Matching of controls

To ensure comparability, we divided start of TCM care into three phases: early (up to 14 days after onset of symptoms), delayed (14–27 days after onset) and late (≥ 28 days after onset). We used patients' gender, age, presence or absence of comorbidities, highest LDH level and worst respiratory status at the first administration of TCM as markers for identifying controls, so that the times at which the latter two markers occurred were similar in patients and controls. The comorbidities included were chronic obstructive airway disease, ischaemic heart disease, cerebrovascular disease, cancer, diabetes, chronic renal failure and chronic liver disease (1, 2). To minimize bias and retain the relative weighting of the case groups, we performed 1000 rounds of random one-to-one bootstrap sampling to match controls (3–6). A total of 107 matched controls were successfully obtained for 24 of the patients treated with TCM. The clinical profiles of the matched patients are listed in Table 2. The patients for whom no controls could be identified are listed in Table 3, with reasons for the non-availability of matched controls.

Symptoms and signs according to Traditional Chinese medicine

A list of TCM symptoms was specifically requested and ranked by the TCM physicians, as listed in Table 4.

Treatment with Traditional Chinese medicine

Treatment was individualized and independent of patients' concurrent Western medical care. Chinese medicine decoctions were prepared at a single TCM pharmacy located in Kwong Wah Hospital.

Clinical decision-making

Only the attending Western medicine physicians decided the dosage and duration of steroid treatment. These physicians also made the decisions regarding discharge of patients, admission to the intensive care unit, duration of stay in intensive care and intubations.

Table 2. Profiles of 24 patients with whom controls were matched

	Time between onset of symptoms and start of treatment with Traditional Chinese medicine (days)			
	Early (<14)	Delayed (14-27)	Late (≥28)	Total
Age (years)				
21-40	3	1	7	11
41-60	4	4	4	12
61-80	1	-	-	1
Sex				
Female	6	4	7	17
Male	2	1	4	7
Comorbidity^a				
No	6	5	10	21
Yes	2	-	1	3
Acute respiratory distress syndrome	2	2	4	8
Mean lactate dehydrogenase reading	635.33	672.25	1064.4	5
Mean age (years)	43.63	43.2	37.55	40.75
Mean days from symptom onset to start of treatment with Traditional Chinese medicine	9.25	16.4	39.64	24.67
Mean days from admission to start of treatment with Traditional Chinese medicine	7.88	15.4	38.55	23.5

^aComorbidities included: chronic obstructive airway disease, ischaemic heart disease, cerebrovascular disease, cancer, diabetes, renal failure and chronic liver disease.

Table 3. Reasons why 24 patients treated with TCM were not matched with controls

Reasons	No of patients	Deaths
Patients were discharged within 5 days after start of TCM care. They recovered well but the duration of TCM treatment was too short. Although they had excellent outcomes, they were not included in the analysis	5	0
Incomplete records of LDH / respiratory status because patients were from different hospitals	4	0
Patients were very ill (ARDS and very high LDH levels). They were the most seriously ill SARS patients and no comparable controls were identified	7	5
Unable to match: no controls with the appropriate combination of LDH and respiratory status within the same age, sex and comorbidity group were identified. These subjects may have represented a unique clinical subgroup of SARS patient	8	2
Total	24	7

TCM, Traditional Chinese medicine; LDH, lactate dehydrogenase; ARDS, acute respiratory distress syndrome.

Table 4. Symptoms and signs recorded in traditional Chinese medicine

Q1	fever	Q19	cough
Q2 ^a	sweating	Q19a	nature of cough
Q2.1	nature of sweat	Q19b	time of cough
Q3	headache	Q20 ^a	sputum
Q4	dizziness	Q20a	ease of expectoration
Q5 ^a	weakness	Q20b	colour of sputum
Q6 ^a	tiredness of limbs	Q20c	nature of sputum
Q7 ^a	tremor	Q21 ^a	capacity of stomach
Q8 ^a	numbness	Q21a	anorexia
Q9	muscle spasm	Q21b	eats a lot; frequent hunger
Q10	sensation of mouth	Q22	epigastric fullness
Q10a ^a	dry mouth	Q23	stool
Q10a.1	desire to drink	Q23a ^a	loose stool
Q10b ^a	thirst	Q23b	dry stool
Q10b.1	preference of drinking	Q23c	sticky stool
Q10c	tastelessness	Q24 ^a	urination
Q10d	sticky sensation in mouth	Q25 ^a	menstrual status
Q11 ^a	palpitations	Q25a	last menstrual period
Q12 ^a	dysphoria	Q25b	menstruation affected by present illness
Q13	dysphoric feverishness	Q26	body build
Q14	hotness of 5 centres	Q27	tongue texture
Q15 ^a	insomnia	Q28	tongue coating
Q16 ^a	sensation of oppression in chest	Q29	tongue body
Q17	shortness of breath	Q30	tongue condition
Q18 ^a	dyspnoea	Q31	pulse

^aOnly these symptoms showed significant improvement after TCM treatment.

Statistical analysis

Percentages were compared by the chi-squared test, and distributions of risk scores were compared by the chi-squared test for goodness of fit. Continuous and ranked data were compared by the t-test and Wilcoxon rank-sum test, respectively. Within-subject improvement in symptoms before and after TCM treatment was compared by the Wilcoxon sign-rank test. A statistically significant difference was defined by a *p*-value of < 0.05. Unless specified, all *p*-values were two-sided. We used commercially available software (SPSS 10.0 and SAS 6) for the statistical analysis.

Results

SARS patients who received TCM were characterized by a higher risk profile than that for all SARS patients in Hong Kong SAR (*p* < 0.01). The death rate of SARS patients who received TCM was not significantly different from that in matched controls (Table 5). However it was clear (Table 5) that patients who were treated with TCM benefited from a significant decrease in the quantity of steroid used.

Table 5. Comparison of progress of illness in SARS patients with that in matched controls

	TCM+ WM Mean (SD)	WM Mean (SD)	Comment
Total stay (days)	36 (2.602)	38.8 (1.53)	NS
ICU stay (days)	15.1 (3.67)	11.03 (1.21)	$P < 0.05$
Duration of intubation (days)	12 (3.01)	8.45 (1.30)	$P < 0.05$
Total dose of steroid used (MG)	22 920 (1968)	30 736 (1862)	$P < 0.05$
Duration of steroid treatment (days)	24.4 (2.14)	28.25 (1.09)	$P < 0.05$
Duration of fever $\geq 38^{\circ}\text{C}$ (days)	8.7 (1.89)	6.62 (0.77)	$P < 0.05$
Death rate	37.5%	30.7%	NS
Intubation rate	41.7%	41.9%	NS
ICU admission rate	50.0%	51.6%	NS
Number of cases	24	107	

TCM, Traditional Chinese medicine; WM, Western medicine; SD, standard deviation; ICU, intensive care unit; NS, no significant difference.

Table 6. Comparison between survivors of SARS and matched controls

	TCM+ WM Mean (SD)	WM Mean (SD)	Probability
Total stay (days)	32.7 (3.47)	36.9 (1.53)	< 0.05
ICU stay (days)	7.06 (4.49)	3.08 (0.62)	< 0.05
Intubation (days)	3.66 (3.316)	2.2 (0.561)	< 0.05
Total steroid use (mg)	16230 (1618.9)	22519(2398.5)	< 0.05
Steroid treatment (days)	22.26 (1.93)	25.46 (1.13)	< 0.05
Fever ($\geq 38^{\circ}\text{C}$) period (days)	6.3 (3.31)	5.34 (0.408)	< 0.05
Number of cases	15	83	

TCM, Traditional Chinese medicine; WM, Western medicine; ICU, intensive care unit.

The characteristics of the survivors are presented in Table 6. On average, survivors of SARS who received TCM benefited by needing a shorter hospital stay (4 days shorter, $p < 0.05$), and by requiring less steroid (a total dose of 16 000 mg versus 22 000 mg; $p < 0.05$) than the corresponding controls. Patients who received TCM also needed a shorter duration of steroid treatment than did controls. It is also noteworthy that although patients treated with TCM stayed longer in the ICU and were intubated for a longer period, they had a shorter total stay in hospital and received less steroid.

We observed that the shortening of hospitalization occurred mainly in TCM patients who first received TCM < 28 days after onset of symptoms (24.2 days for subjects in the TCM-treated group and 28.6 days for controls). For patients who received TCM treatment > 28 days after onset of symptoms, the duration of hospital stay was not significantly different from that of controls (49.9 days for the TCM-treated group and 51.2 days for controls). The benefit of requiring less steroid treatment for TCM-treated patients was observed in all patients regardless of when TCM treatment started.

Table 4 shows that after TCM treatment, patients showed a significant improvement in many TCM symptoms, including tiredness, shortness of breath, loose stools, insomnia and dry mouth.

Discussion

Up to now, Western medicine has been the conventional medicine provided in public hospitals in Hong Kong SAR. TCM is not a routine service to which patients at public hospitals can have access as of right. The provision of TCM care to inpatients in Hong Kong SAR during the SARS outbreak was therefore a special and novel arrangement.

TCM care became available to SARS patients in public hospitals 2 months after the start of the outbreak. The policy governing the access to TCM and the delayed provision of TCM care resulted in there being a group of TCM users who were more seriously ill than the average SARS patients at the time they first received TCM. Our results could not therefore be used to evaluate the effect of TCM on the full spectrum of SARS patients, and they are not strictly comparable with results from China where TCM treatment was started early on in the course of the disease.

To avoid bias, the parameters considered in this study were largely related to decisions made by the practitioners of Western medicine attending the patients. TCM physicians did not interfere with decisions on the duration of hospital stay, admission to the ICU or dosage of steroid. We consider that this arrangement ensured the objectivity of our results.

Some of the TCM patients in this study represented the most seriously ill SARS patients in Hong Kong SAR, and therefore no comparable controls were available for analysis.

Because the patients in this study were from several hospitals, there were some variations in the patterns of investigation, treatment and documentation among the TCM patients. This led to insufficient data for the matching of controls in four cases. In preparation for possible future outbreaks, a standard clinical pathway would greatly help statistical comparison between various treatment regimes, particularly for new diseases such as SARS for which there was no consensus on treatment.

The majority of patients requested TCM care at least 2 weeks after onset of their symptoms. It has been shown that SARS patients in Hong Kong harboured a high viral load mainly during the first week of the disease, whereas the later stage of the disease may be characterized by immune-mediated disorders (7). Therefore the timing of provision of TCM care may have an impact on the outcome of the disease. In this study, the effect of early TCM treatment could not be investigated. However, the observation that patients receiving TCM needed a shorter period of hospitalization applied to patients who first received TCM < 28 days after the onset of symptoms. This suggests that earlier provision of TCM care may be still more beneficial to SARS patients.

The decrease in the total quantity of steroid used in the patients treated with TCM is sizeable. There was also a shortening of the duration of steroid treatment for the patients treated with TCM relative to their matched controls. These observations suggest that TCM may also be useful in conditions that have conventionally required prolonged treatment with high doses of steroids.

We observed no adverse effects of treating SARS patients with TCM, but rather symptoms were improved. Some of the improvements may be related to decreased steroid usage. This observation suggests that TCM may have potential use in relieving the side-effects of steroid treatments.

The need to provide TCM care for SARS patients created the first opportunity for TCM to be used at the ward level of public hospitals in Hong Kong SAR. It also marked the first step in the official recognition of TCM and in the functional integration of Western medicine and TCM in the public hospitals of Hong Kong SAR.

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