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Consequences of MRSA carriage in nursing home residents

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SUMMARY

A prospective cohort study with 1 year follow-up evaluated the relation between MRSA carriage and mortality, likelihood of hospitalization and functional status in residents of a nursing home for the elderly. Included were all 447 residents living in the home in early June 1994. From all patients, swabs were taken from nose, throat and perineum. Additional swabs (sputum, urine or wounds) were taken when indicated. The relative risk (RR) of dying within 6 months in MRSA carriers compared to non-carriers was 2·29 (95% CI = 1·04–5·04). This RR remained stable (1·57–2·40) after adjustment for co-variables using Mantel–Haenszel stratified analysis. After 1 year, the RR was reduced to 1·30 (95% CI = 0·65–2·58). Univariate survival analysis confirmed a difference in survival between carriers and non-carriers after 6 months (log-rank $P = 0{\cdot}04$) and no difference after 1 year. Cox regression analysis resulted in a hazard ratio for dying within 6 months of 1·73 (95% CI = 0·72–4·17). No relation was found between carriage and either likelihood of hospitalization or indicators of functional status. These results are compatible with a possible relation between 6 months mortality and MRSA carriage in nursing home patients. It calls for a large scale, multicentre cohort study in order to either confirm or refute these findings.

INTRODUCTION

Occurrence and clinical significance of MRSA (methicillin resistant *Staphylococcus aureus*) colonization have been studied and reported extensively in hospital settings [1–5]. Data with respect to the clinical consequences of MRSA carriage in nursing home residents however, are scarce and contradictory [6–10]. Moreover, most of the published studies come from US Veterans Administration institutions with their typical setting and population and are not representative for free-standing nursing homes [11]. In different countries different policies with regard to the acceptation or refusal of colonized patients may relate to the differences in point prevalence between countries. In our view, information about the possible influence of MRSA carriage on mortality and morbidity is essential for those having to decide if MRSA positive patients can be accepted within a home for the elderly and if specific measures to treat MRSA carriers and to prevent its spread are needed.

Therefore, a cohort study was performed in one of the larger nursing homes in Belgium to examine mortality, likelihood of hospitalization and functional status in MRSA carriers compared with non-carriers,

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adjusted for basic characteristics, morbidity and functional status at baseline.

METHODS

Patients

Included were all 447 residents living in the Institute Remy in early June 1994 from whom cultures could be obtained. The institute is one of the larger nursing homes in Belgium with 449 residents and almost 170 nursing staff. It consists of two major sections, one for relatively independent aged people (minor care, $n = 139$) and the other for people needing intensive caring (major care, $n = 310$). At the start of the study the male/female ratio was 1/3 and the mean age was 85 years (range: 56–103); 61% of the patients were ambulatory, 37% chairbound and 2% bed ridden. Incontinence was a problem for 227 (51%) patients of whom 10 had a urinary catheter in situ [12].

Baseline data

Age, sex, type of unit (major or minor care) and time since the last hospitalization were taken from the administrative files. The presence of some concurrent diseases (cardiovascular or lung diseases, skin ulcers, other skin diseases, diabetes or cancer) was copied from the medical/nursing files, together with the presence of incontinence (continent, incontinent, catheter in situ), the mobility (ambulant, chairbound, bedridden), the degree of disorientation in time and space on a five item scale from well to totally disoriented, treatment with antibiotics during the last 4 weeks and reason for death or hospitalization if indicated.

Within 1 week, swabs were taken of the nose, throat and perineum from all residents. This was accompanied by sputum collection in case of productive lung disease, by urine collection in case of fever, actual signs of urinary infection or an indwelling urinary catheter, and by wound swabs in case of a skin ulcer. All swabs were taken with a dry cotton swab and transported to the University Hospital Microbiological Laboratory within 3 h. Perineal swabs were inoculated directly on Mannitol Salt agar (0306-01-0-Difco) and on Tryptone soy agar (Lab 11 – Lab M) with 5% horse blood. The plates were incubated and examined for growth of staphylococci after 24 and 48 h. Swabs from nose and throat were inoculated in a staphylococcal enrichment [13] broth on arrival and incubated overnight. The next day subcultures were made on Tryptone soy agar with 5% horse blood that were examined for growth of staphylococci after 24 and 48 h. Susceptibility of all *S. aureus* isolates for methicillin were determined on Mueller Hinton agar (lab 39 – lab M) supplemented with 13 g/l agar and 2 g/ml oxallin by spot inoculation. All incubations were performed at 30 °C.

In accordance with present guidelines [14], all staff were instructed to carefully follow handwashing routines. No further measures were taken to prevent spread or to eradicate colonization. A patient was considered a MRSA carrier if at least one of the cultures showed a positive result.

Outcome data

Mortality as well as first hospitalization and their causes were registered per month for a period of 1 year. The information was retrieved from the nursing homes's file. As an indicator of functional status, degree of mobility, as well as disorientation in time and space, were estimated 6 and 12 months after baseline measurement.

Analysis

The relation between MRSA carriage and death/hospitalization during the follow-up period of 3, 6, 9 and 12 months was assessed by estimating the relative risks (RR) with their 95% confidence interval (95% CI) for mortality/hospitalization in carriers versus non-carriers. Relevant results were adjusted for each of the above mentioned baseline co-variables separately, using Mantel–Haenszel stratified analysis. Interaction with type of unit (major versus minor care) was tested by comparing crude and adjusted relative risks and by calculating a χ^2 test for interaction. A possible relation between MRSA carriage and indicators for functional status was assessed using Pearson's χ^2 test. A possible relation between MRSA carriage and causes of death or hospitalization within the follow-up period was tested using χ^2 test. Causes were classified as either cardiovascular, respiratory, infection, cancer-related or other.

Separate Kaplan–Meier survival curves were produced for carriers and non-carriers to compare

time to death/hospitalization. Censor events consisted of death (for the hospitalization analysis only) or reaching the end of the follow-up period (June 1995). Survival times in both groups of patients were compared using the log rank test.

A Cox regression model was fitted to adjust for the main baseline characteristics: gender, age, presence of concurrent diseases, incontinence, mobility, and degree of disorientation. Epi-Info software was used for basic statistical analysis and SAS for survival analysis.

RESULTS

At baseline, MRSA was present in 32 (7·2%) residents, MSSA in 167 (37%). On average, MRSA carriers were 2 years younger than non-carriers ($P < 0·05$).

No relation was found between MRSA carriage and gender, presence of cardiovascular diseases, diabetes, skin disease other than skin ulcers, or cancer, use of antibiotics during the last 4 weeks (both all antibiotics and broad spectrum antibiotics only) or time since the last hospitalization. There was no significant difference between the prevalence rates in the major and minor care sections.

MRSA carriage was significantly more frequent in patients with lung diseases (RR = 2·23) or skin ulcers (RR = 5·47) and in chair-bound residents compared with either fully ambulatory or bedridden patients (RR = 2·90). There also was a positive relation with urinary incontinence (RR = 2·66) and even more with the presence of an in-dwelling urinary catheter (RR = 8·21). A more extensive report on determinants and spread has been published previously (12).

Crude data analysis and stratified analysis

Of 32 MRSA carriers, 6 died within 6 months and 7 within 12 months. Of 415 non-carriers, 34 died within 6 months and 70 within 12 months. The relative risk of dying within 6 months in carriers compared to non-carriers was 2·29 (95% CI = 1·04–5·04). It remained stable between 1·57 and 2·40 after adjustment for the above-mentioned baseline characteristics using Mantel–Haenszel stratified analysis (Table 1). There was no support for a significant difference between major and minor care units (χ^2 test for interaction, $P = 0·12$). The estimated fraction of mortality attributable to MRSA carriage in this population was 8·4%.

Table 1. *Relative risk of dying within 6 months in MRSA carriers versus non-carriers, adjusted for baseline characteristics using Mantel–Haenszel stratified analysis*

Co-variable	RR	95% CI	Woolf's χ^2 (P-value)*
Gender	2·24	1·01–4·54	0·38
Age group†	2·36	1·08–5·16	0·08
Section‡	1·99	0·91–4·32	0·12
Mobility	1·62	0·74–3·53	
Incontinence	1·53	0·71–3·29	0·44
Disorientation/time	1·80	0·84–3·85	—
Disorientation/space	1·82	0·85–3·92	—
Antibiotics	2·21	1·00–4·86	0·46
Heart disease	2·30	1·05–5·02	0·76
Lung disease	2·08	0·93–4·67	0·55
Skin ulcer	1·93	0·90–4·17	0·17
Other skin disease	2·48	1·12–5·52	0·06
Diabetes	2·20	1·00–4·83	0·57
Malignancies	2·01	0·93–4·35	0·67

* Test for heterogeneity between strata.
† More or less than median age.
‡ Major/minor care.

Table 2. *Relation between MRSA carriage and death/hospitalization within 3, 6, 9 and 12 months (relative risks based on crude data analysis)*

	Relative risk	95% CI
Death		
3 months	2·05	0·64–6·55
6 months	2·29	1·04–5·04
9 months	1·44	0·67–3·09
12 months	1·30	0·65–2·58
Hospitalization		
3 months	2·36	1·07–5·21
6 months	1·57	0·83–2·98
9 months	1·18	0·63–2·21
12 months	1·04	0·56–1·94

After 12 months, the relative risk of dying in carriers compared with non-carriers was 1·30 (95% CI = 0·65–2·58) (Table 2).

Eight carriers and 66 non-carriers were hospitalized within 6 months, 8 carriers and 100 non-carriers within 12 months. The relative risk of hospitalization in carriers compared with non-carriers was 1·57 (95% CI = 0·83–2·98) after 6 months and 1·04 (95% CI = 0·56–1·94) after 12 months (Table 2).

There was no significant relation between MRSA carriage and indicators of functional status after a follow-up period of 6 or 12 months (P-values between

Table 3. *Relation between MRSA carriage and reason for death/hospitalization within 12 months*

Follow-up period	Causes of death or hospitalization (number of carriers/non-carriers)					
	Cancer	Cardio-vascular disease	Infection	Trauma	Other	Total
Death						
3 months	1/4	1/6	1/4	0/0	0/4	3/18
6 months	3/8	1/11	1/6	0/0	1/8	6/33
9 months	3/13	1/18	1/11	0/0	1/10	6/52
12 months	3/19	2/23	1/14	0/0	1/11	7/67
Hospitalization						
3 months	3/8	1/1	1/7	0/6	1/8	6/30
6 months	4/10	1/5	1/11	1/15	1/21	8/62
9 months	4/11	1/8	1/16	1/18	1/29	8/82
12 months	4/13	1/8	1/19	1/21	1/33	8/94

P-values of χ^2 tests on the relation between MRSA carriage and cause of death/hospitalization were $> 0{\cdot}10$ for all periods and all causes.

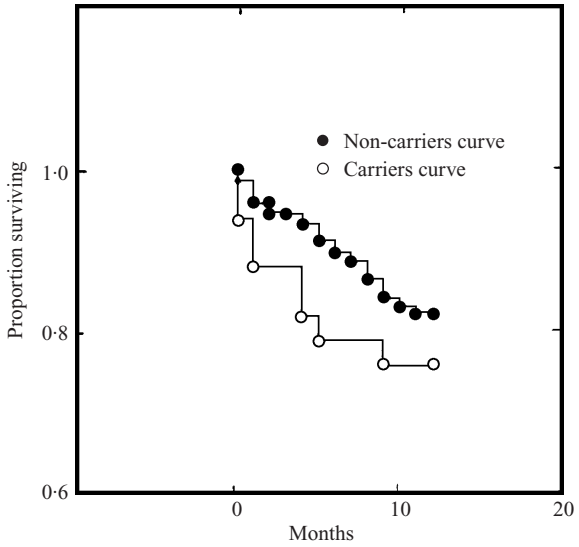

Fig. 1. Survival curve for dying: MRSA carriers versus non-carriers.

0·14 and 0·67). No relation was found between MRSA carriage and cause of death ($P = 0{\cdot}31$) or hospitalization ($P = 0{\cdot}11$) during the follow-up period (Table 3).

Survival analysis

A significant difference in survival between MRSA carriers and non-carriers was found for the first 6 months period (log-rank $P = 0{\cdot}04$), non-carriers having a longer survival rate than carriers. The difference disappeared during the second half year (log-rank $P = 0{\cdot}29$ after a period of 12 months) (Fig. 1).

Cox regression analysis

The Hazard Ratio of dying during a follow-up period of 6 months for carriers versus non-carriers was 1·73 (95% CI = 0·72–4·17). Based on the likelihood ratio χ^2, the *P*-value was 0·0001. Using a follow-up period of 12 months, the Hazard Ratio was 1·17 (95% CI = 0·54–2·52) with a likelihood ratio *P*-value of 0·36.

DISCUSSION

The results of this study suggest an increased 6-month mortality for MRSA carriers living in a nursing home for aged people, compared to non-carriers. The prevalence of MRSA colonization (7·2%) was lower than found in Birmingham or than reported from a number of studies in the US and higher than in the Netherlands where admission rules are extremely restrictive [6–10, 12, 15–17].

Although a lot of information is available on the occurrence, determinants and consequences of MRSA carriage in hospital settings, only a few studies have addressed these questions within nursing homes for the elderly [6–10, 12, 15–17]. The general feeling is that within the general population MRSA disappear quickly and without any consequences for the (ex)-carrier and that nursing home residents can be considered as part of the general population. By their age, nursing home residents are more vulnerable, however, than other people, their degree of multi-morbidity is larger, some of them have an increased likelihood of re-hospitalization and they tend to live together in rooms and wards that are more or less

crowded, compared to the general population. Maybe these factors can help to explain the somewhat unexpected results of our study.

Initially, we tried to explain the excess mortality during the first 6 months by increased vulnerability at baseline. Chronic morbidity is a determinant for MRSA carriage as well as for mortality, and thus a possible confounder for the relation between MRSA carriage and mortality. So are a large number of other characteristics. After adjusting for a large list of these indicators of initial vulnerability, statistical significance of the relation remained at Mantel–Haenszel analysis, during which each co-variable was added separately. It disappeared when using Cox regression analysis, which could be explained by the relatively small power of our study. In this type of complex analysis, the magnitude of the adjusted point estimate however, is stable at crude data as well as multivariate analysis. It should be kept in mind however that multivariate analysis is never an absolute proof for the presence or absence of confounding [18].

It would be dangerous to formulate firm conclusions from one study. Our results however, do not support the hypothesis of absence of an independent cause and effect relation between MRSA carriage and excess mortality during the first 6 months after baseline measurement. They therefore call for further research in this field, including a large scale multicentre cohort study.

At least until the results of such study become available, current guidelines [14], promoting systematic handwashing procedures and discouraging systematic treatment or isolation of carriers should be followed.

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