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Vasectomy and Non-Fatal Acute Myocardial Infarction: A Hospital-Based Case-Control Study in Seoul, Korea

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During 1983–1986, we conducted a hospital-based case-control study in the Republic of Korea to examine the possible relationship between vasectomy and cardiovascular morbidity in men.

One hundred and sixty-three Korean men aged 35–64 who were admitted to a university-affiliated hospital diagnosed for the first time with acute myocardial infarction (AMI) were compared with 326 matched non-AMI patients hospitalized with a diagnosis considered unrelated to vasectomy. When other potentially confounding variables were controlled for, vasectomized men were found to be 2.6 times (adjusted odds ratio) more likely to have had an AMI as compared to the non-vasectomized men (95% CL: 1.1, 6.1). The adjusted odds ratio of AMI for subjects having had a vasectomy ≤9 years ago was the same as those who had a vasectomy ≥15 years (OR=2.5), although those who had had a vasectomy 10–14 years ago were associated with a higher odds ratio of 4.2. Among those subjects with vasectomies who were also cigarette-smokers and/or hypertensive, the risk of development of AMI increased multiplicatively compared with those with none of these conditions. We suspect that our finding of this positive association may be spurious due to possible bias introduced during selection of controls and during the process of data collection. Cancer patients may have been less likely to undergo an elective surgical procedure such as vasectomy prior to the admission. When multivariate analysis included only controls who were non-cancer patients (N=241 controls), the adjusted odds ratio between vasectomy and hospitalization for AMI was reduced to 2.1, (95% CL: 0.8, 5.7), which is no longer statistically significant. When the analysis was further limited to only those control subjects admitted with a diagnosis of digestive system problems, the adjusted odds ratio was reduced to close to unity (1.1).

Recognizing the importance of the study topic and the fact that all previous epidemiological studies showed no association between vasectomy and cardiovascular diseases, we urge further studies. A historical cohort study in the Korean setting is considered feasible and is recommended.

Results from animal studies published in 1978 and 1980 suggest that in rhesus and cynomolgus monkeys, vasectomy may accelerate atherosclerotic changes.[1,2] Subsequently more than a dozen epidemiological studies in humans have been conducted,[3-17] and none has found an association between vasectomy and the development of cardiovascular diseases (CVD). All of these epidemiological studies except one[16] were carried out in the west, and the World Health Organization (WHO) urged that similar studies be conducted in developing countries.[18] We, thus, initiated this study in the Republic of Korea where a widely accepted national vasectomy programme has been in place since 1960 (7.2% of Korean males aged 35 to 64 years had vasectomies by 1982)[19] and where CVD has become the leading cause of death in the adult male population.[20]

The Korean study consisted of two components: a community-based study of cardiovascular deaths and a hospital-based study of non-fatal cardiovascular morbidity, both using a case-control approach. The results of the community based study in which cardiovascular death in Korean men was not found to be associated with vasectomy status have been reported, and the strengths and limitations of the data considered in detail.[21]

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TABLE 1 *Number and vasectomy prevalence (per 100 men) of the 326 controls matched to 163 non-fatal acute myocardial infarction cases according to diagnosis, The Korean hospital-based study, 1983–86*

Diagnosis	Total controls		Prevalence of vasectomy	
	No.	%	No.	Prevalence
Digestive system diseases	165	50.6	17	10.3
Neoplasms	85	26.1	4	4.7
Injury, poisoning, infection or parasitic diseases	30	9.2	4	13.3
Respiratory system diseases	15	4.6	0	0.0
Immune diseases	10	3.1	0	0.0
Nervous system diseases or musculoskeletal disorders	10	3.1	1	10.0
Others*	11	3.4	0	0.0
Total	326	100.0	26	8.0

*Others include: genitourinary system diseases (2), ill-defined conditions (2), mental disorder (3) and miscellaneous (4).

The purpose of the hospital-based study was to determine whether there is a causal association between vasectomy (especially vasectomy a long time ago) and subsequent hospitalization due to CVD, and, if so, whether the effect of vasectomy is potentiated in subjects with their predisposing coronary risk factors such as smoking and hypertension.

The hospital-based study offered greater accuracy of diagnosis than the community-based study, and instead of interviewing the wives of the deceased men and of the controls as surrogates for their husbands, as we did in the community-based study, information was directly obtained from the cases and controls. Data collection was initiated about the same time as the community study (winter of 1983), but ended later in September 1986. Cases included in the hospital-based study were men diagnosed for the first time with ischaemic heart disease (IHD, N=352, ICD-9 codes = 410–414), cerebrovascular disease (N=51, ICD=433–436 and 437.0) and diseases of arteries, arterioles and capillaries (N=4, ICD=440–442, 443.1, 443.9 and 444). Among the 352 IHD patients, 163 were diagnosed with acute myocardial infarction (AMI, ICD=410), 157 with angina pectoris (AP, ICD=413) and the remaining 32 patients with other forms of acute or subacute IHD (ICD=411). For the purpose of this report we limited our study to AMI only, because of its more reliable diagnosis.

METHODS AND MATERIALS

Study Subjects

Recruitment of study subjects was carried out in ten teaching hospitals, all except one located in Seoul. To qualify for entry to the study, cases and controls had to be currently married male patients, aged 35–64 years, with at least one living son. Their wives could not be sterile due to tubal ligation or hysterectomy nor have chronic conditions contraindicating pregnancy or contraception.

Cases were the 163 men hospitalized with a diagnosis, established before discharge, of a first episode of AMI. The WHO criteria were used for the diagnoses.[22] However, for most cases, angiogram, treadmill test and enzyme tests were also perfomed to ascertain the diagnosis. The interviewers were instructed to recruit all patients meeting the criteria, but AMI patients who died on arrival or during their stay at the hospital were excluded. The mean age of these 163 AMI patients was 53.7 years (SD 7.7 years).

Control candidates were male hospital admissions who had no history of myocardial infarction, angina pectoris or any other forms of CVD, and were admitted with a disease not suspected of being related to vasectomy and/or any known effect of a chronic immune response (eg rheumatoid arthritis and idiopathic thrombocytopenic purpura).

Two controls were matched with each case by hospital (same), age (±5 years), number of living children (1–3, 4+), hospital payment status (private or public ward patient) and admission date (closest). All 163 cases were successfully matched with two controls. The mean age of the 326 controls was 52.6 years (SD: 7.3 years). The admission diagnoses of the controls included: digestive system diseases (50.6%); neoplasms (26.1%); injury, poisoning, infection or parasitic diseases (9.2%); respiratory system diseases (4.6%); immune diseases (3.1%); nervous system diseases and musculoskeletal diseases (3.1%); and others (3.4%). Table 1 shows the number and prevalence of vasectomy in controls by diagnosis.

Data Collection and Study Variables

The interviewers, after training, used a structured questionnaire to obtain the following relevant infor-

TABLE 2 *Vasectomy status among the 163 non-fatal acute myocardial infarction case-control triplets. The Korean hospital-based study, 1983–86*

Vasectomy prevalence			No. of triplets
Case	Control I	Control II	
Yes	Yes	Yes	1
Yes	No	Yes	
Yes	Yes	No	6
Yes	No	No	22
No	Yes	Yes	2
No	No	Yes	
No	Yes	No	14
No	No	No	118

Unadjusted odds ratio = 2.78; 95% confidence limits = 1.48–5.20. Odds ratio and CLs were computed by a univariate method allowing for matched sets.[23]

mation from the convalescent patients, for the time up to the onset of the diseases leading to the patient's admission: patient characteristics (birth date, religion, education, occupation, etc), family history in relation to heart attack and/or stroke, reproductive history, lifestyle (cigarette smoking, alcohol consumption and dietary habits, etc) medical history (diagnoses of hypertension, diabetes, hypercholesterolaemia, etc). Vasectomy status was sought twice, first in an open-ended question on the couple's contraceptive history (vasectomy was not specifically mentioned) and then around the end of the interview in a series of closed questions about the patient's experience with six mostly 'minor' surgical procedures including vasectomy, tonsillectomy, appendectomy, gall bladder removal, herniorrhaphy and prostate removal. If the answer to vasectomy was positive to either of these two questions, then age at and place of vasectomy were obtained.

All interviews were conducted in hospital and mostly with patients themselves, 82.8% for cases and 86.8% for controls. In 10.4% of the cases and 9.2% of the controls, the wives answered for the patients, and for two cases and one control, other relatives answered for the patients. This information was missing for the remaining 21 subjects.

Data Analysis

Methods used in data analysis in the present study were generally similar to those used in our community-based study.[21] The independent variables were dichotomized for analysis as follows: age (35–54 versus 55–64); education (≤12 versus 13 or more years); occupation held prior to this admission (professional or administrative versus others); working condition (heavy physical labour versus others), cigarette smoking (ever versus never); alcohol intake (regular versus irregular or never); coffee drinking (every day versus less often or never); lifetime dietary pattern (more meat versus more vegetable); regular leisure time exercise leading to sweating (yes versus no); body weight (Quetelet index based on patient's weight and height measured at admission, dichotomized as <23 versus 23+); histories of physician-diagnosed hypertension, hypercholesterolaemia or diabetes mellitus, all as present or absent (absent including never being examined by a physician); and history of cardiovascular death or sudden death in parents as present or absent. Known important risk factors for IHD such as cigarette-smoking and hypertension were further analysed by more detailed stratification.

Unadjusted odds ratios and their 95% CLs were first calculated, using a univariate method allowing for matched sets,[23] to estimate the overall relative risk of vasectomy as well as other risk factors for AMI in Korean men. Then, the independent effect of vasectomy on AMI was evaluated by adjusted odds ratios, using a conditional logistic regression model allowing for matched sets[23,24] controlling for the effect of the other delineated AMI risk factors either one at a time (always simultaneously controlling for age) or simultaneously. To test the possible duration effect of vasectomy with AMI, we again used the conditional logistic regression model with AMI as the dependent variable and the interval since vasectomy as the independent variable; years since vasectomy was stratified (<10 years, 10–14 years and 15 or more years).

Finally, the possible synergistic effect between vasectomy, cigarette smoking, and hypertension was examined. Odds ratios with 95% CLs (two-tailed) excluding one were considered statistically significant.

All odds ratios cited in this paper allowed for matched triplets, unless otherwise specified. If no risk factors were controlled for, whether using the univariate method or the regression model, the odds ratios are referred to as 'unadjusted'; any time risk factors were controlled for in the regression model, the odds ratios are referred to as 'adjusted'.

RESULTS

History of Vasectomy as a Risk Factor for AMI

Twenty-nine (17.8%) of the 163 cases but only 26 (8.0%) of the 326 controls reported having had a vasectomy. Table 2 shows that for one triplet, all three members reported vasectomy and in 118 triplets, none reported vasectomy. Among the remaining 44 discordant triplets, there were 22 triplets in which the case reported vasectomy, but neither of the control members did. In contrast, there were only two triplets in

TABLE 3 *Unadjusted odds ratios (ORs) and 95% confidence limits (CLs) of potential risk factors of non-fatal acute myocardial infarction (other than vasectomy) for Korean men. The Korean hospital-based study, 1983–86*

Risk factors	No. of triplets studied**	No. of discordant triplets	Unadjusted OR	95% CIs
Age (55+ years/<55 years*)	163	33	2.38	1.13– 5.02
Education (13+ years/<13 years*)	162	104	2.13	1.40– 3.24
Occupation (professional or administrative/others*)	163	89	1.63	1.06– 2.52
Heavy physical labour (yes/no*)	158	62	0.36	0.19– 0.67
Cigarette smoking				
(Ever-smoker/never smoker*)	163	57	2.38	1.24– 4.57
(Former smoker/never smoker*)			1.45	0.65– 3.24
(Currently smokes <1 pack/never smoker*)			2.14	1.07– 4.26
(Currently smokes 1–2 packs/never smoker*)			3.51	1.68– 7.30
(Currently smokes >2 packs/never smoker*)			6.11	2.10–17.78
Alcohol intake (regular/irregular or never*)	161	110	0.57	0.38– 0.87
Dietary habit (more meat/more vegetable*)	160	122	2.62	1.77– 3.90
Coffee drinking (every day/less frequently or never*)	161	116	3.07	2.01– 4.70
Regular leisure time exercise leading to sweating (yes/no*)	161	70	0.56	0.34– 0.90
Quetelet index (23+/<23*)	151	97	1.66	1.10– 2.49
Hypertension				
Diagnosis (yes/no*)	163	86	5.23	3.17– 8.63
Medication (yes/no*)†	159	53	6.17	3.19–11.90
Diagnosis of high cholesterol (yes/no*)	161	24	10.00	3.42–29.26
Diagnosis of diabetes (yes/no*)	153	36	1.96	1.04– 3.66
Parental deaths of CVD or sudden death (yes/no*)	162	107	1.17	0.79– 1.75

*Reference groups.
**Numbers of triplets differed among variables because of some unknown values for these variables.
†Those diagnosed as hypertensive but were not taking medication were pooled with the 'no' group.

which both the control members reported vasectomy and the case did not. The unadjusted odds ratio of AMI for men with vasectomies relative to those without vasectomies was 2.8 (95% CLs: 1.5, 5.2). The average age at vasectomy was 37.3 years for the cases and 35.6 years for the controls.

Other Risk Factors for AMI

Increased risk of AMI was also found among those who were older than 55 years,* had a college education, had a professional or administrative occupation, were an ever or current smoker† (a clear dose-response relationship was shown in current smokers), preferred eating meat to vegetables, were a regular coffee drinker, were overweight, and/or had been told by their physician they were hypertensive, hypercholesteraemic or diabetic. In contrast, subjects engaged in occupations involving heavy physical labour or those with daily leisure time exercise leading to sweating and regular alcohol intake‡ experienced a decreased risk of AMI (Table 3). All of these odds ratios were derived without adjustment.

Some of the variables examined in Table 3 may be also related to the study exposure variable (ie the history of vasectomy), and some may be themselves interrelated. We, therefore, used a multivariate logistic regression model[23,24] and measured the effect of vasectomy on AMI after adjustments for these variables as potential confounders.

The Effect of Vasectomy on AMI after Adjustments for Potentially Confounding Variables

As shown in Table 4, compared to men with no history of vasectomy, the adjusted odds ratios of AMI for men with vasectomy range consistently from 2.6 and 3.6 whether controlling for age alone (Panel A) or controlling for age and any one other risk factor (Panel B). When all these potential confounding variables were controlled for simultaneously (Panel C), an adjusted odds ratio of 2.6 for vasectomized men was derived (95% CLs: 1.1, 6.1).

*Cases and controls were matched on age at the outset but with a wide range (±5 years). Matching was not able to take into account the whole age effect.

†Smoking was defined as five or more cigarettes daily and current smoking was defined as smoking until the diagnosis of AMI was made for cases and until admission for controls.

‡Alcohol consumption in Korean men is generally moderate.[25]

TABLE 4 *Evaluation of the effect of vasectomy on non-fatal acute myocardial infarction in Korean men by odds ratios (ORs) and 95% confidence limits (CLs) adjusted for other potential coronary risk factors.* The Korean hospital-based study, 1983–86*

	No. cases/No. controls studied**	Adjusted ORs for vasectomy†	95% CLs
Controlling for:			
A. Age	163/326	3.17	1.66–6.06
B. Age and			
education	163/325	3.10	1.60–6.04
occupation	163/326	3.07	1.60–5.92
working conditions	159/317	2.75	1.40–5.40
cigarette smoking	163/326	3.46	1.78–6.70
regular alcohol use	162/323	3.06	1.58–5.91
dietary habits	163/323	2.93	1.50–5.72
coffee drinking	162/323	2.64	1.34–5.22
leisure time exercise	163/324	2.99	1.55–5.78
Quetelet index	156/307	3.04	1.57–5.88
diagnosis of hypertension	163/326	2.92	1.48–5.79
medication for hypertension	161/320	2.72	1.38–5.38
diagnosis of high cholesterol	163/324	3.55	1.79–7.02
diagnosis of diabetes	159/312	3.10	1.62–5.96
parental death of CVD or sudden death	163/326	3.14	1.64–6.01
C. All covariates‡	148/282	2.57	1.07–6.15

*The breakdown of the variables in categories is similar to those in Table 3 except for working conditions which was broken down as no physical labour, light physical labour and heavy physical labour.

**Strata were entered into the model as triplets or pairs when one control has a missing value. Numbers of cases and/or controls differed among controlling variables because of unknown values.

†Men with no history of vasectomy were used as the reference group. Adjusted odds ratios were derived from a conditional logistic regression model, allowing for matched sets.[23,24] Case-control status is the dependent variable.

‡ Covariates controlled for were all the variables shown in Panel B except medication for hy, rtension.

The Effect of Length of Time after Vasectomy on AMI

As shown in Table 5, although the number of controls was double that of the cases, there were eight cases and only six controls who had had a vasectomy less than ten years ago; the adjusted odds ratio estimating relative risk of AMI was 2.5 (95% CLs: 0.6, 10.1). Vasectomies performed between 10–14 years prior to hospitalization were reported by 11 cases and nine controls with an adjusted odds ratio of 4.2 (95% CLs: 0.9, 19.6). Vasectomies performed 15 or more years before hospitalization were reported by ten cases and ten controls; the adjusted odds ratio was 2.5 (95% CLs: 0.6, 11.6).

Interaction between Vasectomy, Cigarette Smoking and Hypertension

The effect of vasectomy was considered together with cigarette smoking and physician-diagnosed hypertension, the two variables known to be strong AMI risk factors. Cigarette smoking was divided into ever and

TABLE 5 *Odds ratios (ORs) and 95% confidence limits (CLs) of non-fatal acute myocardial infarction by interval since vasectomy, unadjusted and adjusted for other risk factors. The Korean hospital-based study, 1983–86*

Years since vasectomy	No. of cases	No. of controls	Unadjusted ORs**	CLs 95%	Adjusted OR†	95% CLs
No vasectomy*	134	300	1.00	—	1.00	—
<10	8	6	3.14	1.01–9.79	2.53	0.63–10.11
10–14	11	9	3.37	1.26–9.02	4.23	0.92–19.56
15+	10	10	2.69	1.01–7.20	2.53	0.56–11.56
Missing length of exposure	0	1	—	—	—	—
	163	326				

*Reference group.

**Unadjusted ORs and CLs were computed by univariate method allowing for matched sets;[23] data from 163 cases and 326 controls were used.

†Adjusted odds ratios were derived from a conditional logistic regression model, allowing for matched sets.[23,24] Case-control status is the dependent variable. Data from 148 cases and 281 controls were used. Variables that were controlled for are those listed in Panel B of Table 4.

never smokers. Physician-diagnosed hypertension was divided into present (including those under medication) or absent (including those never having seen a physician for a diagnosis of hypertension).

The odds ratio for subjects who had vasectomies and also one of the other two risk factors increased more than the addition of the independent odds ratios. These estimations were, however, generally based on very small numbers of subjects and thus subject to wide fluctuations (Table 6).

DISCUSSION

Our findings on the magnitude and significance of the association between vasectomy and AMI appear to support the hypothesis derived from animal studies that vasectomy accelerates the progression of atherosclerosis[1,2] and that men with vasectomy may be at an increased risk of subsequently developing non-fatal AMI, especially those who also smoke and/or are hypertensive. However, bias must be carefully considered as the possible explanation for this positive finding.

Selection Bias

Selective admission of AMI patients to these hospitals by the physicians conditional on vasectomy status is not likely. Visits to several general practitioners in the city of Seoul prior to the initiation of the present study revealed that none of them were cognisant with the animal studies. A few cardiologists (two of them later participated in the present study) were aware of the studies, but all expressed disbelief in the results. On the medical charts of coronary heart patients in university hospitals, no history of vasectomy was ever recorded.

Information Bias

If cases overreported and/or controls underreported their vasectomy experience, the relative risk for vasectomy will be spuriously inflated. The likelihood of this type of information bias on the interviewee's part was minimal. The subjects regarded our interviewers as hospital staff and were very cooperative during the interview. Since our study hypothesis was not known to the patients, and vasectomy is an important and clear-cut personal event to them, selective recall and/or underreporting, whether purposely or due to memory decay, does not seem likely.

Most hospitals had only one interviewer, and each interviewer interviewed identical proportions of cases and controls, reducing inter-interviewer variation. Interviewers were told during training that this was a general epidemiological study of CVD in Korean men, and vasectomy was not specifically mentioned.

All cases (N=29) and controls (N=26) who reported having had a vasectomy answered affirmatively to both questions enquiring about the study subject's history of vasectomy. Proportions of cases and controls reporting use of other contraceptive method(s) and/or having had other 'minor' surgeries were generally similar, thus further enhancing the validity of the differences in prevalence of vasectomy between the cases and the controls (Table 7).

Confounding Effect

Our results relating to most known risk factors for AMI were, in general, consistent with findings from western studies.[25] After controlling for these potentially confounding variables, whether one at a time or simultaneously, all of the adjusted odds ratios for vasectomy on AMI were around 3.0 (Table 4) and none were substantially different from the unadjusted odds ratio of 2.8.

If an AMI risk factor is part of the causal pathway between vasectomy and AMI and was controlled for in the multivariate analysis, this should reduce the actual magnitude of the adjusted relative risk for vasectomy. Thirteen cases and two controls who had a vasectomy

TABLE 6 *Unadjusted odds ratios (ORs) and 95% confidence limits (CLs) of non-fatal acute myocardial infarction by histories of vasectomy, cigarette smoking and/or hypertension. The Korean hospital-based study, 1983–86*

Vasectomy	Smoking (ever)	Hypertension	No. of cases	No. of controls	Unadjusted ORs*	95% CLs
No	No	No	5	36	1.00**	—
Yes	No	No	1	8	1.34	0.13– 13.99
No	Yes	No	76	227	2.69	1.01– 7.16
No	No	Yes	4	8	3.10	0.67– 14.30
Yes	Yes	No	15	16	7.82	2.29– 26.68
No	Yes	Yes	49	29	15.60	5.15– 47.26
Yes	No	Yes	2	1	16.31	1.14– 234.28
Yes	Yes	Yes	11	11	109.81	11.01–1095.05

*Derived by conditional logistic regression allowing for matched sets.[23,24] Case-control status is the dependent variable.
**Reference group.

TABLE 7 *Reported contraceptive and 'minor' surgery histories by non-fatal acute myocardial infarction cases and controls. The Korean hospital-based study, 1985–86*

	Case N = 163		Control I N = 163		Control II N = 163	
	No.	%	No.	%	No.	%
When asked about contraceptive practices						
Method						
None	96	58.9	116	71.2	117	71.8
Condom	4	2.5	7	4.3	3	1.8
Oral contraceptives	10	6.1	13	8.0	3	1.8
IUD	8	4.9	7	4.3	14	8.6
Vasectomy*	29	17.8	13	8.0	13	8.0
Others	11	6.7	2	1.2	6	3.2
No response	5	3.1	5	3.1	7	4.3
When asked about 'minor' surgical procedures**						
Procedure						
None	115	70.6	132	81.0	128	78.5
Tonsillectomy	5	3.1	0	0.0	1	0.6
Gallbladder removal	4	2.5	3	1.8	3	1.8
Hernia repair	3	1.8	2	1.2	0	0.0
Prostate removal	0	0.0	0	0.0	1	0.6
Appendectomy	19	11.7	17	10.4	20	12.3
Vasectomy*	29	17.8	13	8.0	13	8.0

*The chi-square test comparing the prevalence of vasectomy between the cases and controls resulted in $p = 0.005$.
**There were subjects who had more than one 'minor' procedure. The percentages were calculated using the 163 subjects as the denominator and thus add up to more than 100%.

also reported one or more of the following diagnoses: hypertension, high cholesterol or diabetes. However, the majority (eight) of the 13 cases and both the controls had the condition diagnosed prior to vasectomy. Also, when we actually excluded these 15 subjects from an unmatched univariate analysis, the odds ratio for vasectomy was 2.0 and was still statistically significant (95% CLs: 1.05, 3.99).

Besides the animal studies that suggest an association between vasectomy and atherosclerotic changes,[1,2] a recent report of a longitudinal study on the Framingham offspring revealed the provocative finding of an independent association between interim vasectomy (ie vasectomy during the follow-up period in men with no vasectomy history at entry to the study) and increased total cholesterol.[26] Our findings seem to support such an association between the long-term effect of vasectomy and the development of AMI which was not confounded by other variables. However, our study is the only epidemiological study showing such positive findings and is in conflict with all previous similar studies,[3-17] as well as our community-based case-control study on the relationship between vasectomy and cardiovascular deaths in Korean men.[21] Therefore, further careful scrutiny of our findings is necessary.

Indeed, most of the subjects with vasectomies who were included in the western studies had recently undergone the procedure (ie less than ten years) and manifestation of symptoms and signs of ischaemic heart disease in humans may need a longer interval.[27] There are, however, three historical cohort studies recently reported, two from the US[5,14] and one from China,[16] which include men who had been exposed to vasectomy for a long time. In the study by Massey *et al*,[5] 2318 (21.9%) of the 10 590 subjects with vasectomy had the procedure ten or more years ago. In Perrin *et al's* study,[14] 603 (43.7%) of the 1379 vasectomized subjects had their vasectomy performed 16 or more years prior to the study. In the Chinese study,[16] close to half (47.9%) of the 12 501 vasectomized subjects had been exposed to the procedure for ten or more years. Also, in the recent case-control study by Rosenberg *et al*[15] 160 (48.2%) of the 332 cases with a vasectomy and 184 (32.2%) of the 572 controls with a vasectomy had the operation ten or more years prior to the study.

It also should be admitted that a large-scale case-control study was a new venture in Korea. Many difficulties were encountered during the coordination with participating hospitals, and a number of compromises were necessary during the execution of the study. We suspect that the compromises made in the selection of cases and controls might have introduced bias into the study and distorted our results.

For instance because of the paucity of patients hospitalized for accident, trauma and/or minor surgery who are better control candidates due to their short stay in hospital, we were forced to use patients hospitalized with chronic conditions as control candidates; some of the chronic conditions might have been longstanding, making it less likely for such patients to have undergone an elective procedure such as vasectomy. Eighty-five control subjects in our study were cancer patients. These patients reported a low vasectomy prevalence (4.7%) (Table 1) and hence triplets including them as controls resulted in a high unadjusted odds ratio of AMI (OR=5.8 with 95% CLs: 1.7, 20.4) (Table 8). On the other hand, the vasectomy rate of the remaining 241 controls with other diagnoses was 9.1% (a prevalence rate generally comparable to that of the Korean male adult population as a whole), producing an unadjusted odds ratio of 2.4 (95% CLs: 1.2, 4.8). The odds ratio adjusted for all potential confounders was 2.1 (95% CLs: 0.8, 5.8, not shown in Table 8). In an analysis limited to the 165 controls who were patients with digestive system problems, the unadjusted odds ratio for vasectomy was reduced to 1.8 (95% CLs: 0.8, 4.1) and the odds ratio adjusted for all potential confounders was close to one (OR=1.09, 95% CLs: 0.3, 3.9; not shown in Table 8).

Duration-response relationships are further support for a cause-effect association. Such a relationship was not detectable when we included only the 146 AMI cases, who had a non-cancer patient as one or both controls (N=241). Subjects with vasectomy performed 15 or more years before hospitalization experienced an unadjusted odds ratio of 2.2 (95% CLs: 0.7, 6.5). This was similar to the odds ratio (2.3, 95% CLs: 0.7, 7.5) associated with subjects with vasectomies performed less than ten years before hospitalization (Table 9), a duration usually deemed too short for the pathogenesis of atherosclerosis in humans to demonstrate itself clinically.[27] The unadjusted odds ratio was 3.5 (95% CLs: 1.1, 10.9) for subjects with vasectomies performed between 10 and 14 years before hospitalization. The numbers of cases and controls were too small to perform this comparison while controlling for other potentially confounding variables.

Other potential biases that could have exaggerated the effect of vasectomy on AMI include the possibility of indirect selective referral based on some patient characteristics related to vasectomy. For example, if men from higher socioeconomic strata were more likely to have had a vasectomy and to have been admitted to these teaching hospitals for AMI, then such a bias would exist. Two variables that indirectly measure socioeconomic status (SES), occupation and education, are related to vasectomy status. Twenty per cent of men with professional or administrative occupations had vasectomies versus 8% of those with other types of occupations ($p<0.01$). Sixteen per cent of men with 13 or more years of education had vasectomies versus 9% of those with less than 13 years ($p=0.03$). If the broad categorization of occupation and education accounted for any socioeconomic differences between cases and controls, adjusting for these variables should have controlled for any SES bias.

The mean age at interview was somewhat higher for cases than controls (53.7 versus 52.6) even though the triplets were matched on age by ±5 years. Therefore, the cases had more opportunity before the interview to obtain a vasectomy. On the other hand, the interval between age at vasectomy (for those vasectomized) and age of 'hospitalization' was 0.6 years longer tor the

TABLE 8 *Unadjusted odds ratios (ORs) and 95% confidence limits (CLs) of non-fatal acute myocardial infarction for the association between hospitalization and vasectomy, by category of diagnosis of the 326 matched controls. The Korean hospital-based study, 1983–86.*

Diagnosis of control	Nos. of cases/ controls	Unadjusted OR* for vasectomy	95% CLs
Cancer	68/85	5.84	1.67–20.39
All controls except cancer	146/241	2.36	1.17– 4.75
Digestive system disease only	115/165	1.81	0.80– 4.10
Others**	57/76	3.10	0.96–10.01

*ORs and 95% CLs were derived from a conditional logistic regression model allowing for matched sets.[23] Case-control status is the dependent variable.

**Others include subjects with injury, poisoning, respiratory system diseases and other diagnosis as listed in Table 1.

TABLE 9 *Unadjusted odds ratios (ORs) and 95% confidence limits (CLs) of the acute myocardial infarction cases (and their 241 non-cancer controls) by interval since vasectomy. The Korean hospital-based study, 1983–86.*

	Nos. of		Unadjusted	
Years since vasectomy	cases	controls	ORs**	95% CLs
No vasectomy*	120	219	1.00	—
<10	7	6	2.31	0.70– 7.54
10–14	11	7	3.54	1.14–10.95
15+	8	8	2.18	0.72– 6.54
Missing length of exposure	0	1	—	—

*Reference group.

**ORs and 95% CLs were derived from a conditional logistic regression model allowing for matched sets.[23] Case-control status is the dependent variable.

controls than for the cases. This should have given the controls more opportunity to develop AMI (if related). Effects of both variables (age and interval) in this study should be small and cancel each other out. Also adjusting for age at interview did not change the results (Table 4).

It is also possible that some of our interviewers might have sensed the true purpose of our study and prompted the cases with more intensity than the controls for history of vasectomy. Although the extent of these effects is not measurable, the differences in odds ratios among hospitals (Table 10) suggest such a possibility. Also not all potential AMI risk factors were included in the multivariate analysis. Information on personality type, for instance, was not used because the information obtained in this study was considered inadequate for analysis. Finally, as the number of studies on this topic increases, the probability of a study showing a significant association by chance also increases.

Our community-based study conducted in four cities in South Korea did not detect an association between vasectomy and cardiovascular death in Korean men.[21] In that study, however, stroke was the leading cause of cardiovascular death and only 7% (29) of the 413 deaths reportedly died of ischaemic heart disease. The results thus are not directly comparable to the present study. For the 51 case-control pairs originally recruited in this hospital-based study in which the cases were diagnosed as having cerebrovascular diseases (not included in this analysis), the unadjusted odds ratio for subjects with a history of vasectomy was 1.4, and the 95% CLs were 0.4 and 4.6. This is not statistically significant.

In conclusion, while this hospital-based study ostensibly suggests a positive association between vasectomy and risk of hospitalization for ischaemic heart diseases in Korean men, this association might be due to bias introduced during case and control selection and during execution of the study. Considering the importance of this topic, a historical cohort study is needed and is considered feasible in the Korean setting.

TABLE 10 *Unadjusted odds ratios (ORs) and 95% confidence limits (CLs) for the evaluation of the effect of vasectomy on non-fatal acute myocardial infarction in Korean men by study hospital. The Korean hospital-based study, 1983–86.*

Hospital	No. of triplets	Unadjusted OR* for vasectomy	95% CLs
Seoul National	55	3.17	1.08–9.29
Yonsei	30	1.50	0.42–5.41
All others**	78	3.67	1.35–9.94

*Unadjusted ORs and CLs were computed by a univariate method allowing for matched sets.[23]

**There are 8 other hospitals: Han Yang (3 cases), National Medical Center (14), Sungshim (19), Korea University (8), Kyung Buk University (16), Kyung Buk University (7), Inje in Seoul (2) and Inje in Pusan (9).

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