Association of Serum Total Cholesterol Level with Hospitalized Infection and the Mediation Effect of Statin Use: Findings from a Community-based Cohort in Taiwan

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Background

Serum cholesterol and lipoproteins play important roles in modulating acute inflammatory response and body innate immunity.
However, whether the risks associated with high or low serum cholesterol level, as well as the effect mediated by subsequent statin use, on hospitalized infection morbidity and mortality are unknown.

Methods

In this community-based cohort study, a total of 80,947 volunteers participating in the New Taipei City Health Screening in 2005–2008 were grouped according to their baseline total cholesterol level (< 160, 160-179, 180-199, 200-219, 220-239 and ≥ 240 mg/dl). Participants were followed to their first hospitalization for infection or death after data linkage with the Taiwan National Health Insurance Research Database (NHIRD) and Death Registry. Logistic regression models, adjusted for baseline demographic, lifestyle, socioeconomic factors and comorbidities, was used to evaluate total and direct effect (Odds ratios, ORs) of different total cholesterol categories for overall and individual sites of infection and infection-related mortality using cholesterol level of 180 to 199 mg/dL as reference group. Mediation analysis was performed to assess the indirect effect mediated by subsequent statin use(Fig. 1)

Results

We found a negative association regarding the total effect of serum cholesterol level and the risk of hospitalized infection [ORs from 1.19 (95% CI: 1.09-1.30) to 0.92 (95% CI:0.84,0.99) as total cholesterol from less than 160 mg/dL to greater than or equal to 240 mg/dL], especially the reproductive and urinary tract infection but not infection-related mortality. However, to decompose the total effect into direct effect.
of cholesterol and indirect effect via statin use, higher risks for hospitalized infection were noted in both lowest and highest level of total cholesterol categories [direct effect, OR:1.13 (95% CI:1.03-1.24) and 1.22 (95% CI:1.12-1.33) in category <160 and ≥ 240 mg/dl respectively] (U-shape relationship).
Protective effects mediated by statin use on infection-related morbidity and mortality were found in participants with cholesterol level greater than 200 mg/dl.
The largest mediation was observed in the highest cholesterol level category of ≥ 240 mg/dl with indirect effect (ORs) via statin use 0.89 (95% CI:0.88-0.90), followed by that of 0.96 (95% CI:0.95-0.96) and 0.98 (95% CI:0.98-0.98) in the category of 220-239 and 200-219 mg/dl respectively.

Conclusion

Both high and low level of total cholesterol were associated with higher risks for hospitalized infectious disease and the risk could notably affected and eliminated by the use of statin in participants with cholesterol level greater than 200 mg/dl. Further studies are needed to support the finding.

Table 1. Characteristics of study participants with different Total cholesterol category at study entry (N = 80,947)

Variable	Total cholesterol level (mg/dL)					
	< 160	160-179	180-199	200-219	220-239	≥ 240
Number	8,781	13,915	18,577	17,063	11,740	10,871
Male	35.03	36.01	35.93	35.86	35.41	32.32
Age, mean (SD)	46.59 (12.24)	47.90 (11.71)	49.50 (11.53)	51.03 (11.15)	52.46 (10.89)	53.75 (10.53)
Obesity	4.56	5.42	5.87	6.63	7.50	7.52
Systemic steroid use*	0.60	0.67	0.83	0.71	1.06	1.18
Cigarette smoking	14.31	14.80	14.59	14.42	14.87	14.75
Comorbidities, %						
Diabetes	5.10	5.30	5.68	5.98	6.94	9.65
Hypertension	10.18	11.69	13.34	14.50	15.55	16.28
eGFR						
≥ 90	70.24	65.96	62.29	58.00	54.60	51.26
60-89	26.57	30.92	34.39	38.21	41.07	43.95
<59	3.19	3.11	3.33	3.79	4.33	4.79
Ischemic heart disease	2.97	3.53	3.90	4.10	4.22	3.90
Myocardial infarction	0.11	0.10	0.13	0.13	0.08	0.10
Cardiac dysrhythmia/atrial fibrillation	1.92	1.98	2.00	2.02	1.92	1.87
Congestive heart failure	1.00	0.83	0.78	0.88	1.01	1.11
Stroke	0.92	0.93	0.97	0.77	0.89	0.86
Peripheral vascular disease	0.25	0.33	0.31	0.41	0.27	0.35
Chronic lung disease	6.26	6.04	6.09	6.36	6.65	6.68
Chronic liver disease	5.58	5.72	5.46	5.36	4.92	4.41

* Systemic steroid use >30 days before study entry

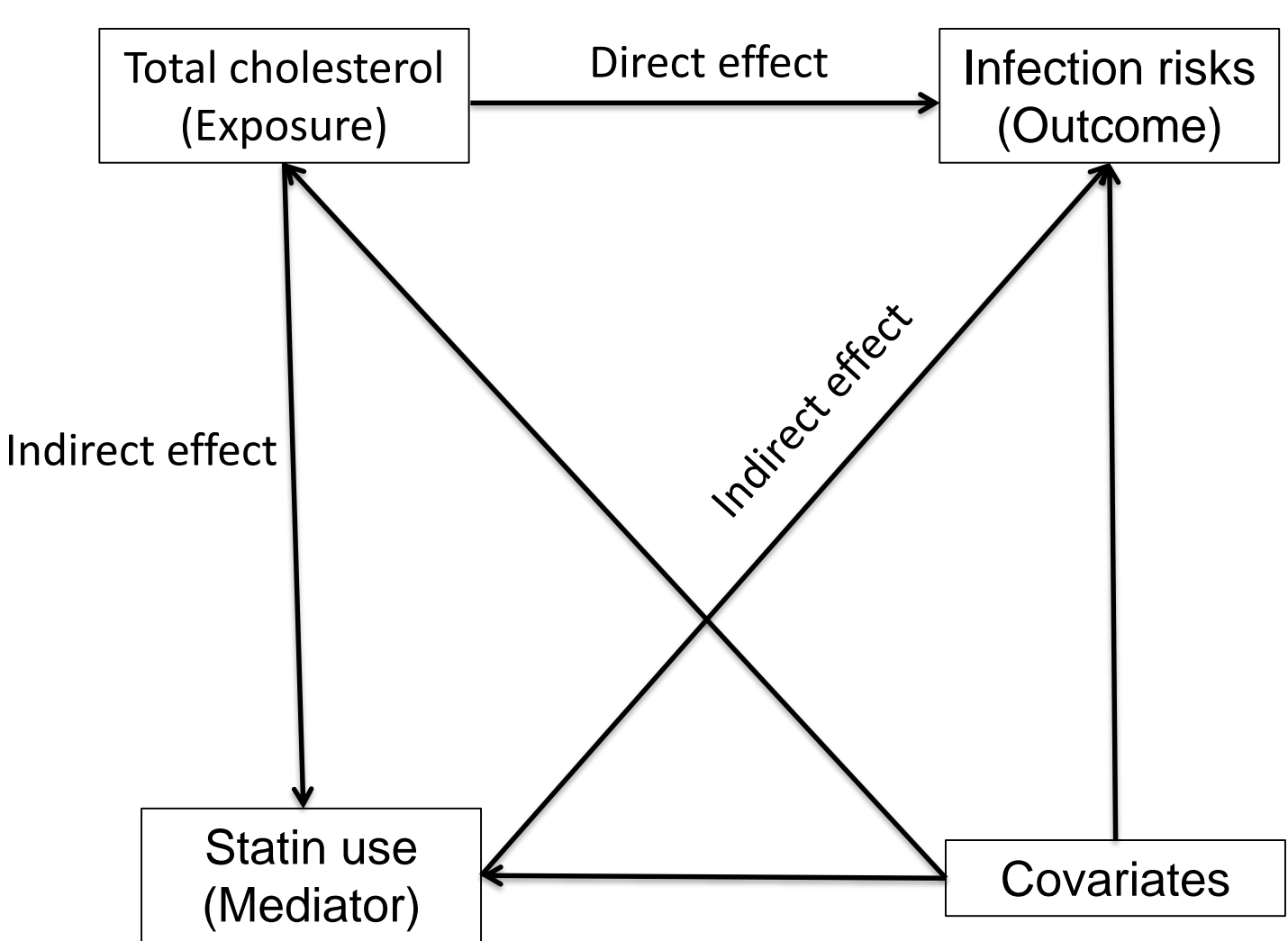Figure 1. Conceptual framework of mediation analysis

Figure 2. The adjusted odds ratios of hospitalization for infection syndrome and infection-related mortality for different total cholesterol categories at baseline as compared with total cholesterol 180-199 (N = 80,947)
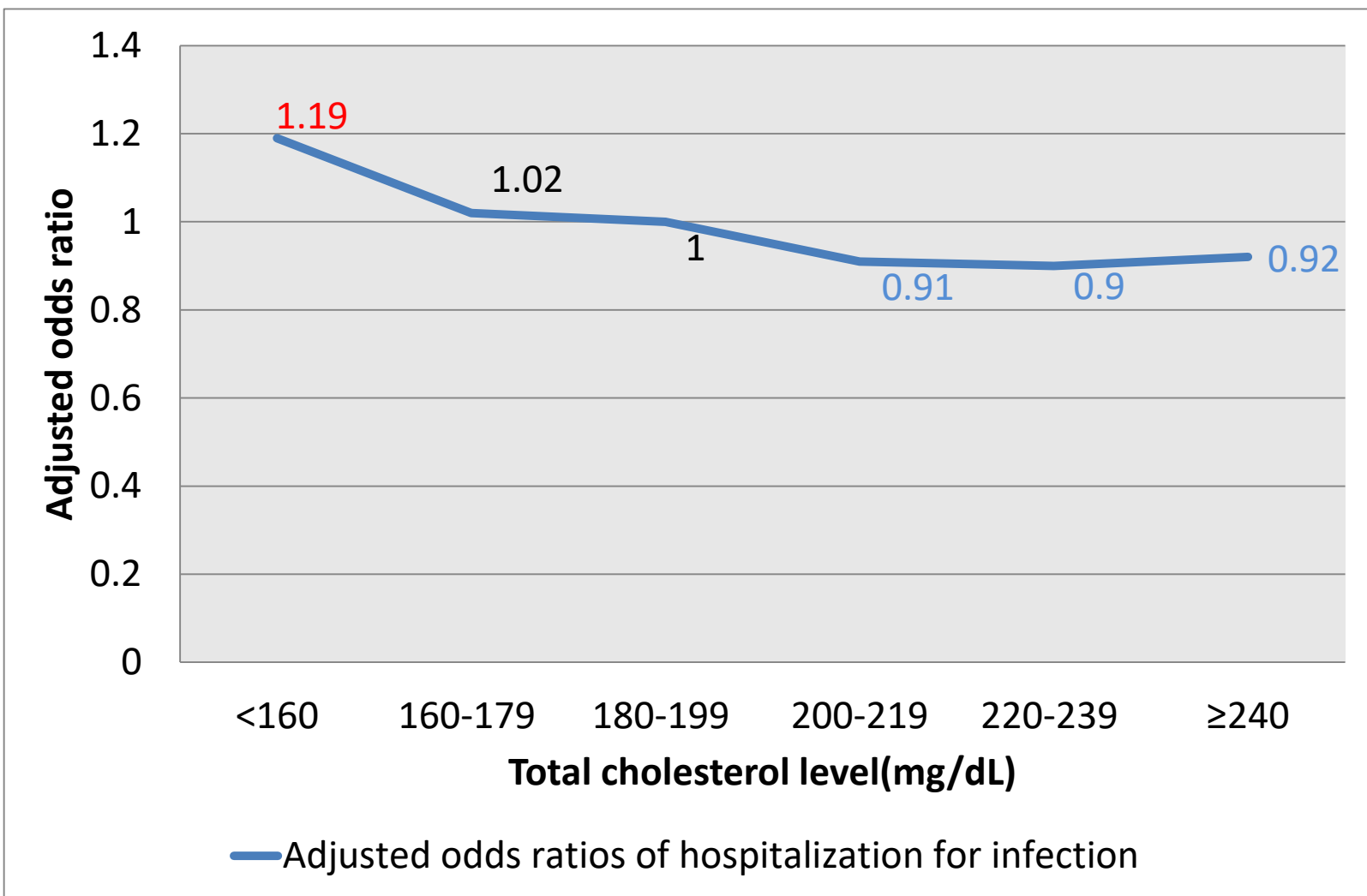

Figure 3. Results of mediation analyses from different total cholesterol levels to each infection through statin (# of bootstrapping=1000), with 95% CI