Short Communication

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Statin use is not associated with inflammation among Chilean women of Mapuche and non-Mapuche ancestry with gallstones

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Aim: Statins are associated with lower risk of gallstones due to anti-inflammatory effects. We assessed whether statins impact circulating inflammation among Chilean women with gallstones. **Materials & methods:** 200 Mapuche women were matched on statin use and age to 200 non-Mapuche women in the Chile Biliary Longitudinal Study. We analyzed 92 inflammatory biomarkers using multivariable-adjusted regression models, random forests and pathway analyses. **Results:** Statins were not significantly associated with any inflammation marker when women were analyzed jointly or stratified by ancestry. No significant associations were found through random forest methods and pathway analyses. **Discussion:** We did not find significant associations between statin use and inflammation markers in women with gallstones, suggesting that statins do not reduce inflammation once gallstones have formed.

Plain language summary: Statins are prescribed to lower cholesterol and can also decrease the risk of gallstone formation by reducing inflammation. We assessed whether statin use reduces inflammation among women who have already developed gallstones. We analyzed 92 inflammation markers among 400 women in Chile, including 200 women with Mapuche Amerindian ancestry and 200 women of Latina/European ancestry. We found that statin use was not correlated with inflammation in this group of women overall nor by ancestry. This may mean that statin use does not reduce inflammation in women who already were diagnosed with gallstones.

First draft submitted: 24 February 2023; Accepted for publication: 18 October 2023; Published online: 11 January 2024

Keywords: Chile • gallstones • inflammation • Mapuche • statins • women

Gallbladder cancer (GBC) is a rare, but lethal cancer with a median survival rate of >1 year [1]. Chile has one of the highest GBC incidences in the world with 5.6 per 100,000 [2]. GBC incidence and mortality in Chile is highest

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for women of Amerindian ancestry, particularly Mapuche women [1,3]. Gallbladder disease is the primary risk factor for GBC resulting in a chronic pro-inflammatory state [4]. Gallstones are also more prevalent among Chilean and Amerindian women who develop gallbladder disease earlier in life with multiple stones more frequently than women in other parts of the world, resulting in prolonged chronic inflammation [4]. Other risk factors for GBC, such as age, hyperlipidemia and obesity also act through inflammatory pathways [4–6].

Inflammation appears to be critical to the development of GBC [4]. The release of inflammatory mediators, including cytokines, chemokines and prostaglandins, into the gallbladder microenvironment promote carcinogenesis through cellular proliferation and apoptosis inhibition [4]. Recently, IL-8 and other inflammatory pathways were identified as important risk factors among Mapuche women with gallbladder disease [7]. Four inflammation protein markers, CCL20, CXCL10, IL-6 and IL-8, were shown to be higher in GBC cases than controls and associated with increased risk of GBC mortality [8,9]. However, these inflammatory biomarkers were assessed in samples collected at GBC diagnosis, so reverse causation is a concern in these studies [8,9].

Statins (3-hydroxy-3-methylglutaryl coenzyme A [HMG-CoA] reductase inhibitors) are widely prescribed to treat hypercholesterolemia. In addition to lowering cholesterol, statins have anti-inflammatory effects by reducing chemokine secretion induced by C-reactive protein [10]. Low-density lipoprotein cholesterol itself induces inflammation and treatment with statins may result in anti-inflammatory actions [11]. Research has shown that statins are associated with a lower risk of gallstones [12] and GBC [13]. Therefore, we sought to assess whether statin use are associated with inflammation marker levels in circulating blood samples overall and by ancestry among Chilean women with gallstones.

Methods

The Chile Biliary Longitudinal Study (Chile BiLS) is a prospective cohort study of Chilean women aged 50–74, with ultrasound-confirmed gallstones, with no prior cholecystectomy (additional details described elsewhere) [14]. The study was approved by institutional review boards of the United States National Cancer Institute, Pontificia Universidad Católica de Chile, and the Chilean Ministry of Health. All participants provided written informed consent and methods were performed in accordance with the relevant guidelines and regulations.

From Chile BiLS, we selected 200 women of self-reported Mapuche ethnicity (plus paternal and maternal Mapuche surname) and 200 women of self-reported Latina/Chilean ethnicity (without Mapuche surname), matched on 5-year age group (50–54, 55–59, 60–64, 65–69, 70–74). Within each ancestry group, 50% were randomly selected self-reported statin users at baseline. Baseline BMI was calculated using measured height and weight, and obesity was defined as BMI $\geq$30 kg/m^2. Self-reported variables in our analysis included a diabetes diagnosis, smoking history, medications, diet, highest level of schooling, and health insurance coverage under Fondo Nacional de Salud (FONASA).

Baseline serum samples (1 µl) were analyzed for 92 biomarkers on the Proseek Multiplex Inflammation I multiplex proximity extension assay panel (Olink Bioscience, Uppsala, Sweden). Relative protein levels were calculated from cycle threshold values with corrections for assay variation and presented as normalized protein eXpression (NPX) on a logarithmic scale. The samples were randomly placed across testing plates and 20 blinded duplicates were included to assess reproducibility within and between plates. All samples had batch coefficients of variation $\leq$5% and intraclass correlations >75%. Our four *a priori* markers of interest (CCL20, CXCL10, IL-6, and IL-8) had intraclass correlations >95%.

All marker values were natural-log transformed; we additionally applied a Box-Cox transformation to AXIN1. Eleven markers were excluded due to low detection (>85% below the lower limit of detect [LLOD]): interferon gamma, IL-1a, IL-2, IL-4, IL-13, IL-20, IL-22RA, IL-33, LIF, TSLP and TNF. The five markers (FGF-5, IL-2RB, ARTN, IL-24 and NRTN) where 50–85% of values were below LLOD were dichotomized as 'detectable' or 'undetectable'. Six markers (FGF-23, IL-5, IL-10RA, IL-17A, IL-17C, IL-20RA) with 10–50% of values below LLOD were categorized into tertiles.

Statistical analyses

Twelve participants were removed due to missing covariates or extreme marker values. Characteristics between statin users and non-users by ancestry were compared using chi-square or t-tests. We used linear regression models to estimate associations between statin use and continuous inflammatory markers and logistic or ordinal regression for categorical markers. All models were adjusted for age, diabetes, waist circumference (measured by study research nurse), smoking status, chili and fried food consumption, education and FONASA group. Results were similar

when models were additionally adjusted for obesity, recruitment method or aspirin use (data not shown). Models were fit overall and stratified by ancestry. For the four *a priori* markers we used $p < 0.05$ and for the others a Bonferroni corrected $p < 0.0006$ (= 0.05/82) was used to determine statistical significance to adjust for multiple testing. Additionally, we stratified analyses by diabetes status among all women and by ancestry.

Because many of the markers were strongly positively correlated (based on Spearman rank correlation), we modeled the markers jointly to understand the relationship between statins and the markers collectively. We used a random forest analysis (R package *randomForest*) that aggregates the predictions made by multiple decision trees of varying depth. In this analysis we used 35 markers including the four *a priori* markers (CCL20, CXCL10, IL-6, and IL-8), the top 20 markers among Mapuche women, and the top 20 markers among non-Mapuche women (with overlap) from the regression analysis. Here we used all markers continuously, with measurements below the LLOD replaced by the LLOD value. Marker importance was assessed using the Gini index.

Olink grouped the inflammation markers into pathways based on biologic functions (https://www.olink.com/products/target/inflammation). We used the ARTP package to obtain pathway-specific summary p-values for associations of each pathway with statin use separately for Mapuche and non-Mapuche women [15]. First, separately for each marker we fit a regression model as described in the first paragraph of the methods section. The p-values for the regression coefficient associated with statin use for all markers in a particular pathway were then combined using an adaptive rank truncated product statistic to obtain a pathway-specific p-value. The statistical significance of the pathway-level p-value (i.e., the test statistic) was evaluated using a highly efficient permutation algorithm obtained by permuting 'statin use' in the regression models and combining the permutation p-values of all markers in the same pathway to obtain a p-value for association of the pathway with statin use.

All analyses were conducted in R (version 4.0.3 [2020-10-10]).

Results

Ninety-nine of the 200 Mapuche women and 100 of the 200 non-Mapuche women were statin users at baseline (Table 1). Among Mapuche women, statin users were more likely to use aspirin or non-steroidal anti-inflammatory drugs (NSAIDs) (38% vs 12%, $p < 0.001$) than non-users. Among non-Mapuche women, statin users were more likely to be obese (61% vs 45%, $p = 0.03$), have diabetes (49% vs 18%, $p < 0.001$), and use aspirin/NSAIDs (44% vs 15%, $p < 0.001$) than non-users. Statin use was not significantly associated with any inflammation marker after multiple comparisons correction among all women combined (Table 2) by ancestry. Multiple-testing-corrected p-values for interaction between statin use and ancestry were not statistically significant (all $p > 0.0006$). Results were similar when models were adjusted for obesity, recruitment method, or NSAIDs/aspirin (data not shown). When models were stratified by diabetes status, among all women and within ancestry, none of the markers reached statistical significance after correcting for multiple comparisons and no differences between strata were observed in marker associations (data not shown).

Jointly analyzing the markers through random forest methods did not identify significant associations with statin use. In pathway analyses, no pathway was associated with statins (all pathway-specific $p > 0.05$; data not shown).

Discussion

In this cross-sectional analysis, statin use was not statistically significantly associated with inflammation markers in Chilean women with gallstones. Statin use was not associated with the inflammation markers, either overall or by ancestry. Statins are commonly prescribed medications used to lower cholesterol (low-density lipoprotein cholesterol and plasma cholesterol) levels among people with hyperlipidemia. Evidence from animal [16] and human [12,17] studies show that statins can decrease the formation and promote dissolution of cholesterol gallstones.

Hyperlipidemia has also been shown to be associated with an increased risk of cancer at all biliary tract sites, presumably by stimulating gallstone formation [5]. In addition to promoting gallstone formation, hyperlipidemia is thought to interact with inflammation and the pro-inflammatory immune response to increase risk of GBC [4,18]. Prolonged cholithiasis results in chronic inflammation, causing the release of inflammatory mediators that may lead to a pro-carcinogenic microenvironment [4]. Inflammatory responses can also vary by ethnicity, as previous research in Chile has reported increased IL-8 inflammatory response in Mapuche women compared with non-Mapuche women with gallstones [19]. Associations have been observed between circulating levels of inflammatory proteins and GBC incidence [8,20] and survival [9].

A previous study by Liu and colleagues found statin use to be associated with a 12% reduction in GBC risk [13]. Additionally, that study found an increasing number of statin prescriptions and cumulative dose were both

10.2144/fsoa-2023-0032

Table 1. Demographic and medical characteristics of Mapuche and non-Mapuche Chilean women by statin use from the Chile BiLS cohort (N = 400).

Characteristic	Mapuche women			Non-Mapuche women		
	Statin use (N = 99)	No statin use (N = 101)	*P*-value †	Statin use (N = 100)	No statin use (N = 100)	*P*-value†
Age, years, mean (SD)	59.4 (6)	59.5 (6)	0.89 §	59.8 (6)	59.7 (6)	0.94§
Education level, n (%)						
– 0–8 years	73 (74)	76 (75)	0.3	44 (44)	52 (52)	0.4
– 9–12 years	23 (23)	19 (19)		46 (46)	42 (42)	
– ≥13 years	2 (2)	6 (6)		10 (10)	6 (6)	
– Missing	1 (1)	0 (0)		0 (0)	0 (0)	
Monthly family income, n (%)						
– ≤CLP $250,000	59 (60)	57 (56)	0.93	56 (56)	49 (49)	0.52
– >CLP $250,000	26 (26)	23 (23)		34 (34)	38 (38)	
– Missing	14 (14)	21 (21)		10 (10)	13 (13)	
Health coverage,‡ n (%)						
– FONASA Group A	54 (55)	61 (60)	0.63	43 (43)	38 (38)	0.64
– FONASA Group B	24 (24)	18 (18)		41 (41)	41 (41)	
– FONASA Group C	1 (1)	2 (2)		5 (5)	5 (5)	
– FONASA Group D	3 (3)	6 (6)		8 (8)	5 (5)	
– Unknown/none	17 (17)	14 (14)		3 (3)	11 (11)	
BMI in kg/m^2, mean (SD)	33.0 (5)	32.6 (6)	0.6 §	32.1 (6)	30.6 (7)	0.07 §
Obese (BMI ≥30 kg/m^2), n (%)	71 (72)	71 (70)	0.95	61 (61)	45 (45)	0.03
Waist circumference in cm, mean (SD)	103.9 (12)	102.5 (12)	0.42 §	99.5 (12)	96.9 (14)	0.14 §
Hip circumference in cm, mean (SD)	111.4 (10)	110.6 (11)	0.62 §	109.3 (11)	107.6 (12)	0.32 §
Diabetes diagnosis, n (%)	32 (32)	22 (22)	0.12	49 (49)	18 (18)	<0.001
Ever smoker, n (%)	3 (3)	7 (7)	0.36	18 (18)	21 (21)	0.72
Gallstones, n (%)						
– 1 stone	28 (28)	43 (43)	0.10	43 (43)	39 (39)	0.37
– ≥2 stones	47 (47)	42 (42)		40 (40)	49 (49)	
– Unknown	24 (24)	16 (16)		17 (17)	12 (12)	
Recruitment method, n (%)						
– Door-to-door contact in urban areas	7 (7)	6 (6)	0.20	22 (22)	16 (16)	0.41
– Local health/community centers, hospitals, media	68 (69)	81 (80)		67 (67)	67 (67)	
– Ultrasonography, surgical consultation and cholecystectomy waiting lists	20 (20)	10 (10)		11 (11)	16 (16)	
– Invitation by local health center	3 (3)	4 (4)		0 (0)	1 (1)	
Diet, n (%)						
– Consumption of fresh green chilis	56 (57)	55 (54)	0.75	40 (40)	41 (41)	0.95
– Consumption of fresh red chilis	41 (41)	37 (37)	0.51	24 (24)	21 (21)	0.73
– Consumption of dried red chilis	35 (35)	31 (31)	0.51	27 (27)	26 (26)	1.00
– Consumption of red chili paste	34 (34)	27 (27)	0.27	22 (22)	26 (26)	0.65
– Consumption of fried food	57 (58)	62 (61)	0.82	51 (51)	53 (53)	0.89
Regular use of Aspirin/NSAID	38 (38)	12 (12)	<0.001	44 (44)	15 (15)	<0.001

†p-value calculated using a chi-square test for the categorical variables except where noted.
‡FONASA groups A-D are hierarchical classifications used to determine the proportion of healthcare costs covered by the government, based on taxable individual income. FONASA Group A has the lowest income level and receives the highest level of governmental coverage of healthcare costs.
§p-value calculated using a *t*-test.
Chile BiLS: Chile biliary longitudinal study; CLP: Chilean pesos; cm: Centimeters; FONASA: Fondo Nacional de Salud (Chile's public health insurance system); kg: Kilogram; m: Meter; n: Number; SD: Standard deviation.

associated with reduced GBC risk [13]. Statins have been shown in a clinical trial to reduce levels of circulating C-reactive protein [21]. In cell and animal models, statins have also been shown to reduce other circulating cytokine levels (e.g., IL-6, IL-8) and inflammatory cell infiltration [22,23]. We hypothesized that statin use might reduce inflammation among Chilean women with gallstones, which could be an important finding for this group who has a high risk of GBC. In the current study, however, all participants have gallstones, and thus, already have a chronic

Table 2. Coefficients for association between inflammation marker and statin use by ancestry estimated from adjusted linear regression models except where noted.

Marker name	All women		Mapuche women		Non-Mapuche women		Interaction p-value
	Estimate	p-value	Estimate	p-value	Estimate	p-value	
CCL20	-0.08	0.41	-0.08	0.56	-0.07	0.58	0.99
CXCL10	-0.04	0.64	-0.01	0.96	-0.05	0.65	0.43
IL-6	-0.14	0.07	-0.14	0.19	-0.13	0.29	0.97
IL-8	-0.08	0.27	0.04	0.70	-0.19	0.06	0.08
ADA	-0.01	0.78	0.03	0.59	-0.03	0.55	0.10
ARTN†	-0.04	0.87	-0.12	0.72	0.00	1.00	0.95
AXIN1	0.00	0.50	0.02	0.04	-0.01	0.19	0.01
Beta-NGF	-0.05	0.04	-0.04	0.31	-0.06	0.09	0.35
CASP-8	-0.02	0.84	0.06	0.51	-0.08	0.49	0.19
CCL11	-0.02	0.72	0.03	0.61	-0.07	0.34	0.17
CCL19	0.04	0.75	0.11	0.48	-0.06	0.71	0.87
CCL23	0.05	0.30	0.05	0.35	0.04	0.59	0.67
CCL25	0.04	0.48	0.13	0.09	-0.05	0.52	0.05
CCL28	-0.07	0.11	-0.04	0.54	-0.12	0.08	0.34
CCL3	0.08	0.18	0.17	0.08	-0.01	0.84	0.07
CCL4	0.03	0.67	0.10	0.28	-0.04	0.64	0.15
CD244	-0.05	0.14	-0.04	0.45	-0.06	0.22	0.45
CD40	0.02	0.59	0.09	0.16	-0.05	0.41	0.04
CD5	-0.01	0.88	0.02	0.71	-0.03	0.51	0.17
CD6	0.02	0.64	0.06	0.37	-0.02	0.82	0.18
CD8A	0.02	0.79	-0.08	0.36	0.10	0.35	0.27
CDCP1	-0.11	0.05	-0.04	0.59	-0.17	0.04	0.21
CSF-1	-0.01	0.62	0.00	0.91	-0.02	0.62	0.56
CST5	-0.02	0.76	-0.01	0.89	-0.03	0.64	0.48
CX3CL1	-0.04	0.41	0.05	0.41	-0.12	0.04	0.01
CXCL1	0.02	0.77	0.04	0.72	0.06	0.60	0.82
CXCL11	-0.02	0.83	0.05	0.71	-0.06	0.64	0.39
CXCL5	-0.03	0.72	-0.09	0.43	0.07	0.56	0.43
CXCL6	0.02	0.81	0.02	0.89	0.06	0.62	0.87
CXCL9	-0.04	0.67	0.05	0.68	-0.09	0.47	0.12
DNER	-0.01	0.64	-0.01	0.70	-0.01	0.86	0.55
EN-RAGE	-0.07	0.50	0.13	0.34	-0.22	0.12	0.02
FGF-19	-0.07	0.44	0.03	0.83	-0.15	0.25	0.16
FGF-21	-0.03	0.74	0.14	0.35	-0.22	0.12	0.12
FGF-23‡	0.33	0.09	0.44	0.11	0.23	0.44	0.42
FGF-5†	0.18	0.41	0.09	0.78	0.27	0.40	0.70
FLT3L	0.05	0.19	0.09	0.09	-0.01	0.94	0.30
GDNF	-0.05	0.22	-0.03	0.64	-0.08	0.12	0.36
HGF	-0.04	0.37	0.05	0.38	-0.12	0.07	0.05
IL-2RB†	0.12	0.62	0.20	0.57	0.00	0.99	0.27
IL-5‡	-0.08	0.68	0.17	0.53	-0.45	0.12	0.12
IL-7	0.03	0.62	0.04	0.63	0.05	0.51	0.62
IL-10	0.00	0.94	0.08	0.19	-0.07	0.35	0.10
IL-10RA‡	-0.13	0.52	-0.36	0.19	0.08	0.78	0.31
IL-10RB	-0.02	0.58	0.02	0.59	-0.06	0.19	0.09

All models are adjusted for age group (50–54, 55–59, 60–64, 65–69, or 70–74 years), waist circumference (continuous), diabetes (yes or no), smoking status (ever or never), education level (0–8, 9–12, or ≥13 years of schooling), health insurance category (FONASA group A, B, C, D, or unknown/none), fresh red chili and fried food consumption.
†Coefficients were estimated with logistic regression.
‡Coefficients were estimated with ordinal regression.

10.2144/fsoa-2023-0032

Table 2. Coefficients for association between inflammation marker and statin use by ancestry estimated from adjusted linear regression models except where noted (cont.).

Marker name	All women		Mapuche women		Non-Mapuche women		Interaction p-value
	Estimate	p-value	Estimate	p-value	Estimate	p-value	
IL-12B	0.03	0.67	0.08	0.35	-0.03	0.73	0.34
IL-15RA	-0.02	0.54	0.01	0.78	-0.04	0.19	0.07
IL-17A‡	-0.05	0.80	0.05	0.85	-0.16	0.57	0.71
IL-17C‡	0.09	0.64	0.11	0.68	0.13	0.64	0.97
IL18	-0.03	0.64	0.13	0.11	-0.22	0.02	0.01
IL-18R1	-0.04	0.33	0.04	0.46	-0.12	0.08	0.03
IL-20RA‡	-0.12	0.56	0.12	0.66	-0.42	0.15	0.15
IL-24†	-0.22	0.46	-0.22	0.62	-0.29	0.49	0.79
LAP-TGF-beta-1	0.02	0.72	0.02	0.81	0.02	0.79	0.93
LIF-R	-0.05	0.06	-0.02	0.55	-0.08	0.03	0.15
MCP-1	0.04	0.44	0.08	0.25	0.02	0.75	0.54
MCP-2	-0.05	0.60	0.05	0.73	-0.11	0.39	0.39
MCP-3	-0.05	0.46	-0.04	0.71	-0.04	0.63	0.73
MCP-4	0.04	0.58	0.11	0.31	0.01	0.95	0.44
MMP-1	-0.09	0.42	-0.06	0.65	-0.13	0.44	0.62
MMP-10	-0.03	0.64	0.00	0.96	-0.03	0.73	0.66
NRTN†	-0.03	0.90	0.41	0.20	-0.65	0.09	0.04
NT-3	-0.05	0.19	-0.02	0.60	-0.08	0.16	0.45
OPG	-0.02	0.51	0.06	0.18	-0.10	0.07	0.01
OSM	-0.13	0.23	0.10	0.48	-0.31	0.05	0.02
PD-L1	-0.04	0.41	0.03	0.73	-0.12	0.09	0.13
SCF	0.11	0.01	0.06	0.24	0.13	0.03	0.42
SIRT2	-0.03	0.82	0.02	0.90	-0.07	0.69	0.54
SLAMF1	-0.13	0.003	-0.10	0.12	-0.15	0.02	0.20
ST1A1	0.01	0.95	0.29	0.04	-0.28	0.10	0.01
STAMBP	0.02	0.79	0.07	0.54	-0.02	0.89	0.40
TGF-alpha	-0.04	0.52	0.08	0.29	-0.15	0.09	0.01
TNFB	-0.01	0.78	-0.05	0.44	0.03	0.58	0.32
TNFRSF9	0.03	0.54	0.10	0.21	-0.04	0.54	0.11
TNFSF14	-0.06	0.48	0.12	0.35	-0.24	0.07	0.02
TRAIL	-0.01	0.66	-0.01	0.83	-0.03	0.40	0.73
TRANCE	-0.10	0.10	-0.13	0.13	-0.10	0.25	0.49
TWEAK	0.04	0.25	0.06	0.13	0.01	0.81	0.30
UPA	-0.05	0.15	-0.02	0.62	-0.07	0.17	0.32
VEGFA	-0.07	0.25	-0.03	0.74	-0.11	0.25	0.51
4E-BP1	0.02	0.88	-0.03	0.87	0.05	0.79	0.87

All models are adjusted for age group (50–54, 55–59, 60–64, 65–69, or 70–74 years), waist circumference (continuous), diabetes (yes or no), smoking status (ever or never), education level (0–8, 9–12, or ≥13 years of schooling), health insurance category (FONASA group A, B, C, D, or unknown/none), fresh red chili and fried food consumption.
†Coefficients were estimated with logistic regression.
‡Coefficients were estimated with ordinal regression.

inflammatory state [4]. It is possible that the presence of gallstones might overwhelm any potential effects of statins on inflammation that might have been observed in a gallstone-free comparison group. Alternatively, the decrease in GBC risk reported by Liu *et al.* may have been driven by the cholesterol lowering effects of, and thus gallstone formation, rather than by statins decreasing inflammation directly once gallstones had formed.

Strengths of our study include the use of surname to classify women by Mapuche ancestry, and detailed information on women's medical history, medications and lifestyle factors related to inflammation. However, we could not adjust for important social and cultural differences between ancestry groups that are related to

inflammation, such as detailed dietary patterns or traditional medicine use. We had limited power to assess differences in marker associations by diabetes status by ancestry. This was a cross-sectional analysis and longitudinal analyses are needed to clarify the role of long-term statin use on inflammation and GBC.

Conclusion

Our findings indicate that we may need to revise our thinking around statins reducing inflammation in women with gallstones. Instead, statin use may reduce the risk of gallstone formation leading to a reduced risk of GBC. Additional work is needed to clarify the biologic mechanisms by which statins decrease the risk of gallbladder disease and GBC. To better understand the mechanism involved, future longitudinal studies could evaluate statin associations with cholesterol levels and within subgroups defined by gallstone status, obesity, and other genetic or environmental factors.

Summary points

- Statin use is associated with lower risk of gallstones and has anti-inflammatory effects.
- We assessed whether statin use was associated with reduced inflammation in a group of Chilean women who were previously diagnosed with gallstones.
- We analyzed 92 inflammatory markers measured in blood from 400 Chilean women, including 200 women of Mapuche Amerindian ancestry and 200 women of Latina/European ancestry.
- Statin use was not associated with any inflammation marker level examined among all individuals or when stratified by ancestry.
- Our results suggest that statin use may not reduce inflammation once gallstones have formed.

Author contributions

Study concept and design: SS Jackson, J Koshiol; acquisition of data: V Van De Wyngard, P Cook, JC Araya, C Ferreccio; analysis and interpretation of data: SS Jackson, M Lex, RM Pfeiffer, LA Pinto, SH Jackson, K Choi, TZ Minas, HF Losada Morales, A Hildesheim, J Koshiol; drafting of the manuscript: SS Jackson, J Koshiol; obtained funding: A Hildesheim, C Ferreccio, J Koshiol; study supervision J Koshiol and RM Pfeiffer.

Financial disclosure

This work was supported by general funds from the Intramural Research Program of the US National Institutes of Health, National Cancer Institute, Division of Cancer Epidemiology and Genetics; the Office of Research on Women's Health, National Institutes of Health; the Comisión Nacional de Investigación Científica y Tecnológica for the Fondo de Financiamiento de Centros de Investigación en Áreas Prioritarias (grant 15130011) and the Fondo Nacional de Desarrollo Científico y Tecnológico (grant 1170395) from the government of Chile; the Facultad de Medicina of the Universidad Católica del Maule; the Facultad de Medicina of the Pontificia Universidad Católica de Chile; and the Universidad de La Frontera. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Competing interests disclosure

The authors have no competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Writing disclosure

No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

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