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History of tonsillectomy is associated with glandular inflammation in Sjögren`s disease

Florian Kollert^{1,2}, Valentina Pucino^{1,3}, Saba Nayar¹, Jason Turner¹, Saaeha Rauz^{1,4}, Andrea Richards⁵, Jon Higham⁵, Ana Poveda-Gallego^{1,4,5}, Rachel M. Brown⁶, Timothy Bates⁵, Simon J. Bowman^{1,3}, Francesca Barone^{1,3} and Benjamin A. Fisher^{1,3}

1. Institute of Inflammation and Ageing, College of Medical and Dental Sciences, University of Birmingham, UK
2. Department of Rheumatology, Immunology, and Allergology, Inselspital, University Hospital Bern, Bern, Switzerland,
3. National Institute for Health Research (NIHR) Birmingham Biomedical Research Centre and Department of Rheumatology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK.
4. Academic Unit of Ophthalmology, Birmingham and Midland Eye Centre, Birmingham, UK.
5. Department of Oral Medicine, Birmingham Dental Hospital, Birmingham, UK.
6. Department of Histopathology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK.

Address for correspondence:

Dr Benjamin Fisher (b.fisher@bham.ac.uk),

Rheumatology Research Group,

Institute of Inflammation and Ageing,

University of Birmingham, Birmingham B15 2TT, UK

Dear Editor,

Sjögren`s disease (SjD) is characterized by B cell hyperactivity and focal lymphocytic infiltration of salivary glands. The palatine tonsils are secondary lymphoid-organs that are a first line of defense against pathogens and a unique inductive site for B cell responses with selective homing to bronchial and nasal mucosae and lacrimal and salivary glands (1).

Tonsillectomy (TE) is a common surgical procedure that is often reported to have little effect on immune function (2) based on short-term studies. However, some studies have shown a

reduction in serum immunoglobulins over time, and a population-based study found TE to be associated with long-term risk of respiratory, infectious and allergic diseases (3).

Further, a recent Swedish population-based study found that TE was associated with increased risk of several autoimmune diseases, including SjD (4). Whether a history of TE is associated with the clinical and immunological phenotype of SjD has not been investigated to date.

New patients under investigation for SjS were recruited into the Optimising Assessment in Sjögren's Syndrome (OASIS) cohort established in Birmingham, UK in 2014 as previously described (5). Participants completed a questionnaire at enrolment that included history of TE and appendectomy (AE). This questionnaire was completed independently of, and subsequent to, clinical assessment. We included 183 participants recruited between 2014-2019 with a diagnosis of SjD (n=116) according to ACR/EULAR 2016 or non-SjD sicca syndrome (n=67). Sicca patients had objective and/or subjective dryness, did not meet ACR/EULAR classification criteria and were anti-Ro/SSA negative and had no physician diagnosis of SjD. One SjD patient who had TE around the time of symptom onset was excluded. All subjects provided written informed consent and the study was approved by the Wales Research Ethics Committee 7 (WREC 7) formerly Dyfed Powys REC; 13/WA/0392.

Age, sex and symptom duration did not differ between SjD and non-SjD sicca (online supplementary table 1). Overall, 29% (53/183) had TE; 24.1% of SjD (28/116) and 37.3% of sicca patients (25/67) ($p=0.043$). The median age at TE was 8 (3-50) years and did not differ between SjS and sicca patients ($p=0.629$). SjD patients with TE showed a higher focus score on biopsy [median 2.1 (range 1.2-2.8) vs. 1.3 (0.0-4.3); $p=0.049$] and were more likely to have activity in the glandular (53.6 vs. 20.5%; $p=0.001$) and constitutional (39.3 vs. 14.9%, $p=0.014$) domains of the ESSDAI, but lower levels of serum IgG [12.2 (7.8-35.6) vs. 15.6 (5.7-56.4) g/l; $p=0.012$] and IgA [2.3 (0.9-6.6) vs. 2.9 (0.7-9.4) g/l; $p=0.032$] (Table 1 and Figure 1). VAS global health was significantly lower in SjD patients with TE (58 (10-78) vs. 70 (10-97); $p=0.021$). SjD patients with TE had a higher BMI. BMI might influence glandular swelling via immunometabolic effects or difficulties in clinical assessment. However, multivariable logistic regression analyses showed that TE was associated with glandular swelling and constitutional symptoms even when adjusted for BMI (OR: 3.88, 95%CI: 1.53-9.8; $p=0.004$ and OR: 4.31, 95%CI: 1.56-11.91; $p=0.005$, respectively supplementary table 5). We observed no differences between sicca patients with and without TE (supplementary table 2). For comparison we analysed AE. With the exception of lower salivary flow in SjD (0.09 (0.01-0.43) vs. 0.11 (0.0-1.3) ml/min; $p=0.026$), and higher age in sicca patients with AE ($p=0.015$) there were no

differences (supplementary tables 3 and 4). We are unable to conclude if TE is a risk factor for the development of SjD or non-SjD sicca based on low numbers and the lack of an appropriate age-matched population-based control cohort with accurate TE data. Moreover, this study is limited by the number of histopathological samples in the TE group (n=9) versus the non-TE group (n=43).

In conclusion, TE was associated with lower IgG and IgA levels in SjD but not sicca implying a specific blunting of SjD associated systemic B cell hyperactivity. Moreover, history of TE in SjD was associated with higher focus scores and with glandular swelling and constitutional symptoms. One hypothesis to explain these findings is that a subtle immunodeficiency following TE was compensated by increased lymphoid tissue genesis in the glands. In fact, it has been established that mice deficient in mucosal secondary lymphoid organs develop more severe chemical-induced colitis characterised by high numbers of local tertiary lymphoid structures. This likely results from impairment of local regulatory immune responses and/or deficiency in anti-bacterial immunity (6) (7). Thus, the absence of normal tonsillar function may enhance a local mucosal inflammatory response within the salivary glands without impacting systemic responses.

As the number of lymphocytic foci are a key criterion in the histopathological assessment of SjD, TE status may be capable of influencing diagnosis and should be considered important information to record when patients first present. These findings also provide a strong rationale to expand this observation in other and larger cohorts as well as to determine mechanistic effects of TE on autoimmunity.

Conflict of Interest

FK is an employee of F. Hoffmann-La Roche, FB is an employee of Candel Therapeutics. All other authors declare no competing interests.

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publication are those of the authors and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health.

Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

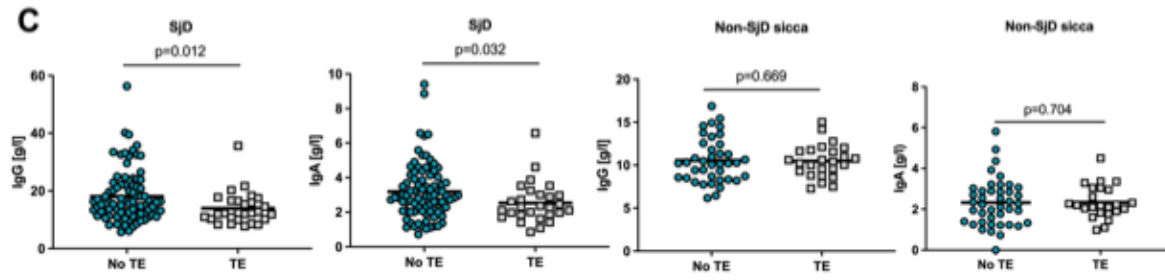
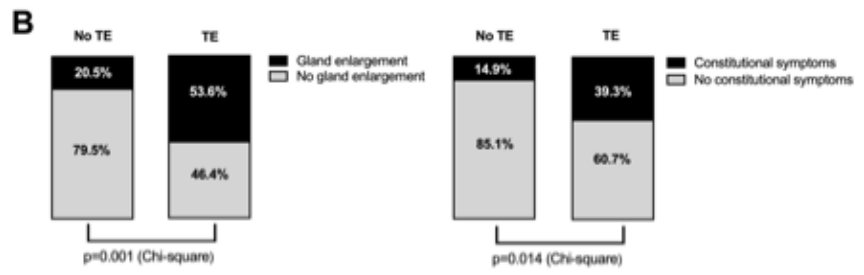
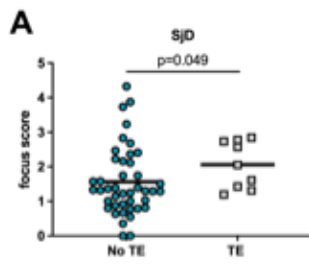
Patient and Public Involvement statement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this study.

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Figure 1: **Phenotype of patients with and without tonsillectomy**. A: histological focus score on minor salivary glands biopsy in SjD with/without TE (n=52); B: glandular enlargement (n=116) and constitutional symptoms (n=115) in SjD with/without TE; C: serum immunoglobulin G and A levels in SjD (n=116/n=115) and sicca (n=67/n=66) with/without TE. *Abbreviations: SjD: Sjögren`s disease; TE: tonsillectomy*



Supplementary Information

History of tonsillectomy is associated with glandular inflammation in Sjögren`s disease

Florian Kollert^{1,2}, Valentina Pucino^{1,3}, Saaeha Rauz^{1,4}, Andrea Richards⁵, Jon Higham⁵, Ana Poveda-Gallego^{1,4,5}, Rachel M. Brown⁶, Timothy Bates⁵, Simon J. Bowman^{1,3}, Francesca Barone^{1,3} and Benjamin A. Fisher^{1,3}

1. Institute of Inflammation and Ageing, College of Medical and Dental Sciences, University of Birmingham, UK
2. Department of Rheumatology, Immunology, and Allergology, Inselspital, University Hospital Bern, Bern, Switzerland,
3. National Institute for Health Research (NIHR) Birmingham Biomedical Research Centre and Department of Rheumatology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK.
4. Academic Unit of Ophthalmology, Birmingham and Midland Eye Centre, Birmingham, UK.
5. Department of Oral Medicine, Birmingham Dental Hospital, Birmingham, UK.
6. Department of Histopathology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK.

Address for correspondence:

Dr Benjamin Fisher (b.fisher@bham.ac.uk),
Rheumatology Research Group,
Institute of Inflammation and Ageing,
University of Birmingham, Birmingham B15 2TT, UK

Supplementary Table 1. Patient`s characteristics Sjögren`s disease and Non-Sjögren`s Sicca

| Variable | n | Sjögren`s disease (n=116) | n | Non-Sjögren`s sicca (n=67) | p-value (Mann-Whitney, Chi-square) |
|-------------------------------|-----|------------------------------|----|-------------------------------|------------------------------------|
| Age at inclusion [years] | 116 | 55.7 (22.7-79.2) | 67 | 59.6 (30.2-80.0) | 0.175 |
| Symptom duration [years] | 109 | 5.7 (0.2-35.6) | 60 | 5.5 (0.6-47.5) | 0.979 |
| Female % (n) | 116 | 94.8 (110) | 67 | 89.6 (60) | 0.234 |
| BMI [kg/m ²] | 114 | 26.8 (18.1-46.8) | 67 | 27.6 (15.7-49.3) | 0.682 |
| UWS [ml/min] | 109 | 0.05 (0-0.67) | 65 | 0.10 (0-1.3) | <0.001 |
| Schirmer`s test [mm/5min] | 105 | 3 (0-40) | 62 | 10 (0-40) | <0.001 |
| Ro/SSA positivity % (n) | 116 | 86.2 (100) | 67 | 0 (0) | <0.001 |
| La/SSB positivity % (n) | 116 | 52.6 (61) | 67 | 0 (0) | <0.001 |
| Focus score | 52 | 1.37 (0-4.32) | - | - | - |
| Focus ≥1 | 52 | 76.9 (40) | 27 | 3.7 (1) | <0.001 |
| IS treatment % (n) | 114 | 33.3 (38) | 67 | 11.9 (8) | 0.001 |
| Gland swelling % (n) | 116 | 28.4 (33) | 66 | 15.2 (10) | 0.030 |
| Lymphadenopathy % (n) | 115 | 2.6 (3) | 66 | 3.0 (2) | 0.602 |
| Constitutional symptoms % (n) | 115 | 20.9 (24) | 66 | 9.1 (6) | 0.030 |
| RF positivity | 108 | 67.6 (73) | 60 | 8.3 (5) | <0.001 |
| IgG [g/l] | 116 | 15 (5.7-56.4) | 67 | 10.2 (6.2-16.9) | <0.001 |
| IgA [g/l] | 115 | 2.73 (0.72-9.4) | 66 | 2.21 (0-5.81) | 0.002 |
| IgM [g/l] | 115 | 1.12 (0.23-9.94) | 66 | 1.04 (0-5.81) | 0.103 |
| C3 [g/l] | 111 | 1.26 (0.79-2.05) | 62 | 1.34 (0.78-2) | 0.088 |
| C4 [g/l] | 112 | 0.22 (0.03-1.34) | 63 | 0.26 (0.09-0.6) | <0.001 |
| β2M [mg/l] | 62 | 2.34 (1.27-4.69) | 44 | 1.81 (1.24-3.08) | <0.001 |
| FLCκ [mg/l] | 94 | 24.9 (7-112) | 60 | 13.2 (7-37) | <0.001 |
| FLCλ [mg/l] | 94 | 19.6 (1-117) | 60 | 12.9 (7-40) | <0.001 |
| ESSPRI | 91 | 6 (0-10) | 61 | 6.3 (1-10) | 0.950 |
| ESSDAI | 116 | 3 (0-29) | 65 | 0 (0-9) | <0.001 |
| EQ5D | 93 | 0.69 (-0.59-1) | 63 | 0.69 (-0.17-1) | 0.244 |
| VAS global patient | 63 | 65 (10-97) | 48 | 65 (24-92) | 0.870 |

Values are shown as median (range) or absolute numbers/percentages. Abbreviations: BMI: body mass index; UWS: unstimulated whole saliva flow; IS: immunosuppressive; RF: rheumatoid factor; β2M: β2-microglobulin; FLC: free light chains; ESSPRI: European League against Rheumatism Sjögren`s syndrome patient-reported index; ESSDAI: European League against Rheumatism Sjögren`s syndrome disease activity index; EQ5D: EURO-QOL 5-dimension; VAS: visual analogue scale.

Supplementary Table 2. Patient`s characteristics Sjögren`s disease with and without tonsillectomy

| Variable | n | Sjögren`s disease Tonsillectomy | Sjögren`s disease No tonsillectomy | p-value (Mann-Whitney, Chi-square) |
|-------------------------------|-----|------------------------------------|---------------------------------------|------------------------------------|
| Age at inclusion [years] | 108 | 56.4 (29.6-76.4) | 54.8 (22.7-79.2) | 0.122 |
| Symptom duration [years] | 109 | 2.6 (0.4-26.1) | 6.1 (0.2-35.6) | 0.623 |
| Female % (n) | 116 | 92.9 (26/2) | 95.5 (84/4) | 0.630 |
| BMI [kg/m ²] | 114 | 29.3 (18.2-49.8) | 26.4 (19.1-44.8) | 0.019 |
| UWS [ml/min] | 109 | 0.04 (0.0-0.29) | 0.05 (0.00-0.67) | 0.740 |
| Schirmer`s test [mm/5min] | 105 | 2 (0-23) | 3 (0-40) | 0.515 |
| Ro/SSA positivity % (n) | 116 | 78.6 (22/6) | 88.6 (78/10) | 0.211 |
| La/SSB positivity % (n) | 116 | 42.9 (12/16) | 55.7 (49/39) | 0.280 |
| Focus score | 52 | 2.1 (1.2-2.8) | 1.3 (0.0-4.3) | 0.049 |
| Focus ≥1 | 52 | 100 (9/0) | 72.1 (31/12) | 0.097 |
| IS treatment (y/n) % (n) | 114 | 28.6 (8/20) | 34.9 (30/56) | 0.647 |
| Gland swelling % (n) | 116 | 53.6 (15/28) | 20.5 (18/70) | 0.001 |
| Lymphadenopathy % (n) | 115 | 7.1 (2/26) | 1.1 (1/86) | 0.146 |
| Constitutional symptoms % (n) | 115 | 39.3 (11/17) | 14.9 (13/74) | 0.014 |
| RF positivity | 108 | 63 (17/10) | 69.1 (56/25) | 0.636 |
| IgG [g/l] | 116 | 12.2 (7.8-35.6) | 15.6 (5.7-56.4) | 0.012 |
| IgA [g/l] | 115 | 2.3 (0.9-6.6) | 2.9 (0.7-9.4) | 0.032 |
| IgM [g/l] | 115 | 1.0 (0.3-2.9) | 1.2 (0.2-9.9) | 0.187 |
| C3 [g/l] | 111 | 1.2 (0.8-1.8) | 1.3 (0.8-2.1) | 0.770 |
| C4 [g/l] | 112 | 0.2 (0.03-0.93) | 0.2 (0.03-1.3) | 0.962 |
| β2M [mg/l] | 62 | 2.39 (1.31-3.52) | 2.31 (1.27-4.69) | 0.717 |
| FLCκ [mg/l] | 94 | 22.6 (8-79) | 25.9 (7.0-112.0) | 0.065 |
| FLCλ [mg/l] | 94 | 18.5 (1-117) | 19.8 (8-58) | 0.554 |
| ESSPRI | 91 | 6.0 (2.7-10) | 6.3 (0-10) | 0.996 |
| ESSDAI | 116 | 5 (0-22) | 3 (0-29) | 0.274 |
| EQ5D | 93 | 0.69 (0.03-1.0) | 0.69 (-0.59-1.0) | 0.718 |
| VAS global patient | 63 | 58 (10-79) | 70 (10-97) | 0.021 |

Values are shown as median (range) or absolute numbers/percentages. Abbreviations: BMI: body mass index; UWS: unstimulated whole saliva flow; IS: immunosuppressive; RF: rheumatoid factor; β2M: β2-microglobulin; FLC: free light chains; ESSRPI: European League against Rheumatism Sjögren`s syndrome patient-reported index; ESSDAI: European League against Rheumatism Sjögren`s syndrome disease activity index; EQ5D: EURO-QOL 5-dimension; VAS: visual analogue scale.

Supplementary Table 3. Patient`s characteristics non-Sjögren`s sicca with and without tonsillectomy

| Variable | n | Non-Sjögren`s sicca Tonsillectomy | Non-Sjögren`s sicca No tonsillectomy | p-value (Mann-Whitney, Chi-square) |
|-------------------------------|----|--------------------------------------|---|------------------------------------|
| Age at inclusion [years] | 67 | 63.3 (36.0-80.0) | 57.7 (30.2-76.5) | 0.091 |
| Symptoms duration [years] | 60 | 5.3 (0.6-26) | 5.5 (0.6-47.5) | 0.873 |
| Female % (n) | 67 | 84 (21) | 92.9 (39) | 0.411 |
| BMI [kg/m ²] | 66 | 28 (18.9-48.3) | 27.5 (15.7-43.9) | 0.890 |
| UWS [ml/min] | | 0.06 (0-0.85) | 0.11 (0-1.3) | 0.434 |
| Schirmer`s test [mm/5min] | 62 | 7 (0-40) | 10 (0-40) | 0.154 |
| Ro/SSA positivity % (n) | 67 | 0 (0) | 0 (0) | - |
| La/SSB positivity % (n) | 67 | 0 (0) | 0 (0) | - |
| Focus ≥1 % (n) | 27 | 7.7 (1) | 0 (0) | 0.481 |
| Gland swelling % (n) | 66 | 16 (4) | 14.6 (6) | 1.000 |
| Lymphadenopathy % (n) | 66 | 4 (1) | 2.4 (1) | 1.000 |
| Constitutional symptoms % (n) | 66 | 8 (2) | 9.8 (4) | 1.000 |
| RF positivity | 60 | 9.1 (2) | 7.9 (3) | 1.000 |
| IgG [g/l] | 67 | 10.4 (7.3-15) | 10.2 (6.2-16.9) | 0.669 |
| IgA [g/l] | 66 | 2.2 (1-4.5) | 2.3 (0-5.8) | 0.704 |
| IgM [g/l] | 66 | 0.9 (0.3-2.9) | 1.1 (0.3-2.7) | 0.182 |
| C3 [g/l] | 62 | 1.3 (0.1-0.6) | 1.4 (0.8-1.9) | 0.410 |
| C4 [g/l] | 63 | 0.3 (0.1-0.6) | 0.3 (0.1-0.5) | 0.858 |
| β2M [mg/l] | 44 | 1.9 (1.2-2.4) | 1.8 (1.3-3.1) | 0.087 |
| FLCκ [mg/l] | 60 | 14.6 (9-37) | 13.1 (7-23) | 0.284 |
| FLCλ [mg/l] | 60 | 13.1 (8-40) | 12.8 (7-23) | 0.826 |
| ESSPRI | 61 | 6.2 (2.7-8.7) | 6.7 (1-9) | 0.702 |
| ESSDAI | 65 | 0 (0-9) | 0 (0-8) | 0.623 |
| EQ5D | 63 | 0.57 (-0.02-1) | 0.69 (-0.17-1) | 0.144 |
| VAS global patient | 48 | 60 (30-85) | 70 (24-92) | 0.583 |

Values are shown as median (range) or absolute numbers/percentages. Abbreviations: BMI: body mass index; UWS: unstimulated whole saliva flow; IS: immunosuppressive; RF: rheumatoid factor; β2M: β2-microglobulin; FLC: free light chains; ESSPRI: European League against Rheumatism Sjögren`s syndrome patient-reported index; ESSDAI: European League against Rheumatism Sjögren`s syndrome disease activity index; EQ5D: EURO-QOL 5-dimension; VAS: visual analogue scale.

Supplementary Table 4. Patient`s characteristics Sjögren`s disease with and without appendectomy

| Variable | n | Sjögren`s disease Appendectomy (n=12) | Sjögren`s disease No Appendectomy (n=102) | p-value (Mann- Whitney, Chi- square) |
|-------------------------------|-----|---|---|--|
| Age at inclusion [years] | 114 | 56.5 (41.7-78.7) | 55.2 (22.7-79.2) | 0.319 |
| Symptoms duration [years] | 107 | 6.8 (1.0-35.6) | 5.6 (0.2-34.4) | 0.574 |
| Female % (n) | 114 | 91.7 (11) | 95.1 (97) | 0.495 |
| BMI [kg/m ²] | 112 | 26.1 (20.6-31.2) | 26.9 (18.2-46.8) | 0.572 |
| UWS [ml/min] | 109 | 0.086 (0.01-0.43) | 0.11 (0.0-1.3) | 0.026 |
| Schirmer`s test [mm/5min] | 104 | 3 (0-16) | 3 (0-40) | 0.802 |
| Ro/SSA positivity % (n) | 114 | 75 (9) | 87.3 (89) | 0.371 |
| La/SSB positivity % (n) | 114 | 66.7 (8) | 50 (51) | 0.365 |
| Focus score | 51 | 1.3 (1.0-2.2) | 1.4 (0.0-4.3) | 0.679 |
| Focus ≥1 | 51 | 100 (6) | 73.3 (33) | 0.315 |
| IS treatment (y/n) % (n) | 112 | 16.7 (2) | 36.0 (36) | 0.217 |
| Gland swelling % (n) | 114 | 16.7 (2) | 29.4(30) | 0.505 |
| Lymphadenopathy % (n) | 113 | 0 (0) | 3.0 (3) | 1.000 |
| Constitutional symptoms % (n) | 113 | 33.3 (4) | 19.8 (20) | 0.278 |
| RF positivity | 107 | 72.7 (8) | 66.7 (64) | 0.487 |
| IgG [g/l] | 114 | 12.7 (8.4-21.7) | 15.1 (5.7-56.4) | 0.234 |
| IgA [g/l] | 113 | 2.6 (1.1-4.9) | 2.8 (0.7-9.4) | 0.918 |
| IgM [g/l] | 113 | 1.5 (0.7-4.9) | 1.0 (0.23-9.9) | 0.081 |
| C3 [g/l] | 109 | 1.22 (0.96-1.65) | 1.26 (0.79-2.05) | 0.578 |
| C4 [g/l] | 110 | 0.22 (0.09-0.93) | 0.2 (0.03-1.34) | 0.598 |
| β2M [mg/l] | 61 | 2.16 (1.31-4.63) | 2.34 (1.27-4.25) | 0.379 |
| FLCκ [mg/l] | 92 | 18.3 (8-44) | 24.8 (7-112) | 0.186 |
| FLCλ [mg/l] | 92 | 17 (7-32) | 19.6 (1-117) | 0.512 |
| ESSPRI | 89 | 6.2 (3-8.7) | 6 (0-10) | 0.740 |
| ESSDAI | 91 | 2.5 (0-17) | 3 (0-29) | 0.654 |
| EQ5D | 91 | 0.69 (0.06-1) | 0.69 (-0.59-1) | 0.864 |
| VAS global patient | 62 | 70 (50-90) | 65 (10-97) | 0.303 |

Values are shown as median (range) or absolute numbers/percentages. Abbreviations: BMI: body mass index; UWS: unstimulated whole saliva flow; IS: immunosuppressive; RF: rheumatoid factor; β2M: β2-microglobulin; FLC: free light chains; ESSRPI: European League against Rheumatism Sjögren`s syndrome patient-reported index; ESSDAI: European League against Rheumatism Sjögren`s syndrome disease activity index; EQ5D: EURO-QOL 5-dimension; VAS: visual analogue scale.

Supplementary Table 5. Patient`s characteristics non-Sjögren`s sicca with and without

| Variable | n | Non-Sjögren`s sicca Appendectomy | Non-Sjögren`s sicca No appendectomy | p-value (Mann-Whitney, Chi-square) |
|------------------------------------|----|-------------------------------------|--|------------------------------------|
| Age at inclusion [years] | 67 | 64.7 (56.5-80.0) | 59.0 (30.2-75.3) | 0.015 |
| Symptoms duration [years] | 60 | 5.5 (2-47.5) | 5.5 (0.5-20) | 0.992 |
| Female % (n) | 67 | 90.9 (10) | 89.3 (50) | 1.000 |
| BMI [kg/m ²] | 66 | 26.9 (15.7-32.5) | 28 (18.4-49.3) | 0.394 |
| UWS [ml/min] | | 0.09 (0.01-0.43) | 0.11 (0-1.3) | 0.820 |
| Schirmer`s test [mm/5min] | 62 | 6.3 (0-40) | 9.8 (0-40) | 0.916 |
| Ro/SSA positivity % (n) | 67 | 0 (0) | 0 (0) | - |
| La/SSB positivity % (n) | | 0 (0) | 0 (0) | - |
| Focus ≥1 % (n) | 27 | 0 (0) | 4.5 (1) | 1.000 |
| Gland swelling % (n) | 66 | 18.2 (2) | 14.5 (8) | 0.668 |
| Lymphadenopathy % (n) | 66 | 0 (0) | 3.6 (2) | 1.000 |
| Constitutional symptoms % (n) | 66 | 9.1 (1) | 9.1 (5) | 1.000 |
| RF positivity | 60 | 0 (0) | 5 (9.8) | 1.000 |
| IgG [g/l] | 67 | 10 (7.3-12.6) | 10.3 (6.2-16.9) | 0.402 |
| IgA [g/l] | 66 | 2.6 (0.7-5.8) | 2.2 (0-4.9) | 0.221 |
| IgM [g/l] | 66 | 1 (0.3-2.2) | 1 (0.3-2.9) | 0.491 |
| C3 [g/l] | 62 | 1.3 (1-1.8) | 1.4 (0.8-2) | 0.983 |
| C4 [g/l] | 63 | 0.3 (0.2-0.4) | 0.3 (0.1-0.6) | 0.694 |
| β2M [mg/l] | 44 | 1.8 (1.2-3.1) | 1.8 (1.3-3.1) | 0.875 |
| FLCκ [mg/l] | 60 | 16 (11-21) | 13.1 (7-37) | 0.184 |
| FLCλ [mg/l] | 60 | 12.3 (8-20) | 13.5 (7-40) | 0.428 |
| ESSPRI | 63 | 7.3 (2.7-10) | 6.3 (1-9) | 0.328 |
| ESSDAI | 65 | 0 (0-9) | 0 (0-8) | 0.784 |
| EQ5D | 63 | 0.52 (0.06-1) | 0.69 (-0.17-1) | 0.670 |
| VAS global patient appendectomy | 48 | 80 (30-91) | 65 (24-92) | 0.398 |

Values are shown as median (range) or absolute numbers/percentages. Abbreviations: BMI: body mass index; UWS: unstimulated whole saliva flow; IS: immunosuppressive; RF: rheumatoid factor; β2M: β2-microglobulin; FLC: free light chains; ESSRPI: European League against Rheumatism Sjögren`s syndrome patient-reported index; ESSDAI: European League against Rheumatism Sjögren`s syndrome disease activity index; EQ5D: EURO-QOL 5-dimension; VAS: visual analogue scale.

Supplementary Table 6. Multivariable logistic regression analysis for glandular swelling and constitutional symptoms

| Variable | Odds ratio | 95%CI | p-value |
|---------------------------------|-------------------|--------------|----------------|
| <i>Glandular swelling:</i> | | | |
| BMI [kg/m²] | 1.05 | 0.97-1.14 | 0.255 |
| Tonsillectomy | 3.88 | 1.53-9.83 | 0.004 |
| <i>Constitutional symptoms:</i> | | | |
| BMI [kg/m²] | 0.97 | 0.88-1.06 | 0.512 |
| Tonsillectomy | 4.31 | 1.56-11.91 | 0.005 |

Abbreviations: BMI: body mass index; CI: confidence interval.