

**Supplementary Table 1.** Comparative semi-quantitative PINA Grading of micro-structural damage of pancreas [PINA]

[Extracted and modified from Gibson-Corley, et al. 2013, Suttie, et al. 2017]

| Features                                   | Grading                                       | Histopathological characteristics of score                                                                                                 | Scoring            | Score |
|--------------------------------------------|-----------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|--------------------|-------|
| <b>P</b> ancreatic<br>Acinar<br>morphology | Normal or<br>No<br>abnormality<br>(score = 0) | Acinar cells: Normal size and morphology with basophilic cytoplasm.                                                                        | Yes = 0,<br>No = 1 |       |
|                                            |                                               | Basally located nuclei, intact lobular architecture                                                                                        | Yes = 0,<br>No = 1 |       |
|                                            |                                               | Absence of necrosis or inflammatory cell infiltration.                                                                                     | Yes = 0,<br>No = 1 |       |
|                                            | Mild acinar<br>damage<br>(score = 1)          | Slight reduction in acinar cell size, decreased cytoplasmic basophilia, or minimal cytoplasmic vacuolation.                                | Yes = 1,<br>No = 0 |       |
|                                            |                                               | Occasional necrotic acinar cells may be present, with sparse inflammatory cell infiltration limited to interstitial or perivascular areas. | Yes = 1,<br>No = 0 |       |
|                                            |                                               | Overall architecture is preserved.                                                                                                         | Yes = 1,<br>No = 0 |       |
|                                            | Moderate<br>acinar damage<br>(score = 2)      | Loss of cytoplasmic basophilia, and increased cytoplasmic vacuolation.                                                                     | Yes = 2,<br>No = 0 |       |
|                                            |                                               | Moderate inflammatory cell infiltration extending into acinar tissue with partial disruption of lobular architecture.                      | Yes = 2,<br>No = 0 |       |
|                                            |                                               | Multifocal acinar cell necrosis.                                                                                                           | Yes = 2,<br>No = 0 |       |
|                                            | Severe acinar<br>damage<br>(score = 3)        | Severe and diffuse acinar damage with marked acinar atrophy or loss.                                                                       | Yes = 3,<br>No = 0 |       |
|                                            |                                               | Extensive acinar cell necrosis, dense inflammatory cell infiltration, and                                                                  | Yes = 3,<br>No = 0 |       |

|                                                         |                                          |                                                                                            |                    |  |
|---------------------------------------------------------|------------------------------------------|--------------------------------------------------------------------------------------------|--------------------|--|
|                                                         |                                          | severe distortion or collapse of acinar architecture                                       |                    |  |
|                                                         |                                          | Presence of fibrous tissue or duct-like structures, replacement of acini by fibrous tissue | Yes = 3,<br>No = 0 |  |
| <b>I</b> nflammation (insulitis)<br>Islet of Langerhans | Normal or No Inflammation<br>(score = 0) | No inflammatory cell infiltration within or around islets.                                 | Yes = 0,<br>No = 1 |  |
|                                                         |                                          | Islet-acinar interface is clean.                                                           | Yes = 0,<br>No = 1 |  |
|                                                         | Mild Inflammation<br>(score = 1)         | Sparse inflammatory cells, mainly at the periphery of the islet (peri-insulitis).          | Yes = 1,<br>No = 0 |  |
|                                                         |                                          | Infiltration is focal and does not distort islet architecture.                             | Yes = 1,<br>No = 0 |  |
|                                                         | Moderate Inflammation<br>(score = 2)     | Clear infiltration of inflammatory cells extending into the islet parenchyma.              | Yes = 2,<br>No = 0 |  |
|                                                         |                                          | Partial disruption of islet architecture, but islet still identifiable.                    | Yes = 2,<br>No = 0 |  |
|                                                         | Severe Inflammation<br>(score = 3)       | Dense inflammatory infiltrate throughout the islet.                                        | Yes = 3,<br>No = 0 |  |
|                                                         |                                          | Marked architectural distortion or destruction.                                            | Yes = 3,<br>No = 0 |  |
|                                                         |                                          | Islet boundaries are poorly defined or lost.                                               | Yes = 3,<br>No = 0 |  |
| <b>N</b> ecrosis of Islet of Langerhans                 | Normal or No Necrosis<br>(score = 0)     | $\beta$ -cells show normal nuclear and cytoplasmic features.                               | Yes = 0,<br>No = 1 |  |
|                                                         |                                          | No necrotic changes.                                                                       | Yes = 0,<br>No = 1 |  |
|                                                         |                                          | Uniform staining and intact cell borders.                                                  | Yes = 0,<br>No = 1 |  |
|                                                         | Mild Necrosis                            | Occasional necrotic $\beta$ -cells with pyknotic nuclei and/or mild cytoplasmic            | Yes = 1,<br>No = 0 |  |

|                                                                               |                                        |                                                                                              |                    |  |
|-------------------------------------------------------------------------------|----------------------------------------|----------------------------------------------------------------------------------------------|--------------------|--|
|                                                                               | (score = 1)                            | eosinophilia.                                                                                |                    |  |
|                                                                               |                                        | Necrosis is focal and limited to a small area of the islet.                                  | Yes = 1,<br>No = 0 |  |
|                                                                               | Moderate<br>Necrosis<br>(score = 2)    | Multiple necrotic $\beta$ -cells observed.                                                   | Yes = 2,<br>No = 0 |  |
|                                                                               |                                        | Prominent nuclear pyknosis, karyorrhexis, or karyolysis.                                     | Yes = 2,<br>No = 0 |  |
|                                                                               |                                        | Increased cytoplasmic eosinophilia.                                                          | Yes = 2,<br>No = 0 |  |
|                                                                               |                                        | Necrosis involves a significant portion of the islet.                                        | Yes = 2,<br>No = 0 |  |
|                                                                               | Severe<br>Necrosis<br>(score = 3)      | Extensive $\beta$ -cell loss showing empty space.                                            | Yes = 3,<br>No = 0 |  |
|                                                                               |                                        | Large areas of the islet show ghost cells, nuclear debris, or complete cellular dissolution. | Yes = 3,<br>No = 0 |  |
|                                                                               |                                        | Architecture of islet is grossly disrupted.                                                  | Yes = 3,<br>No = 0 |  |
| <b>A</b> trophy of<br>Islet of<br>Langerhans<br><br>(Reduction<br>in size and | Normal or<br>No atrophy<br>(score = 0) | Islets are round to oval, well circumscribed.                                                | Yes = 0,<br>No = 1 |  |
|                                                                               |                                        | Normal cellular density.                                                                     | Yes = 0,<br>No = 1 |  |
|                                                                               |                                        | Normal size for age.                                                                         | Yes = 0,<br>No = 1 |  |
|                                                                               |                                        | No obvious shrinkage.                                                                        | Yes = 0,<br>No = 1 |  |
|                                                                               |                                        | Clear distinction from surrounding acinar tissue.                                            | Yes = 0,<br>No = 1 |  |
|                                                                               |                                        | Slight reduction in islet size.                                                              | Yes = 1,<br>No = 0 |  |
|                                                                               |                                        | Mild decrease in cellularity, but islet                                                      | Yes = 1,           |  |

|              |                                 |                                                                           |                    |  |
|--------------|---------------------------------|---------------------------------------------------------------------------|--------------------|--|
| cellularity) | Mild atrophy<br>(score = 1)     | outline still preserved.                                                  | No = 0             |  |
|              |                                 | Overall Islet architecture preserved / maintained.                        | Yes = 1,<br>No = 0 |  |
|              |                                 | Easy to miss unless you compare with control slides.                      | Yes = 1,<br>No = 0 |  |
|              | Moderate atrophy<br>(score = 2) | Obvious reduction in islet size.                                          | Yes = 2,<br>No = 0 |  |
|              |                                 | Marked loss of cellularity with widened intercellular spaces.             | Yes = 2,<br>No = 0 |  |
|              |                                 | Irregular Islet contour with partial loss of architectural integrity.     | Yes = 2,<br>No = 0 |  |
|              |                                 | Endocrine–exocrine distinction starts to blur.                            | Yes = 2,<br>No = 0 |  |
|              | Severe atrophy<br>(score = 3)   | Severely shrunk or collapsed islets.                                      | Yes = 3,<br>No = 0 |  |
|              |                                 | Very few endocrine cells remaining.                                       | Yes = 3,<br>No = 0 |  |
|              |                                 | Islets may appear fragmented or barely recognizable within acinar tissue. | Yes = 3,<br>No = 0 |  |

# Median Score of each of the four grades of histopathological injury (Normal, Mild, Moderate and Severe) were used for the further data analysis in SPSS. [Minimum score = 0 and Maximum Score = 12]  
Group comparisons were performed using the Kruskal-Wallis test.