Supplemental Table 1 – Anthropometric and metabolic characteristics of the study participants.*

	Controls	T2D	*p*°	SGLT2i
n (F/M)	12 (6/6)	13 (7/6)		7 (3/4)
Age (years)	36 ± 10	54 ± 6	<0.0001	31 ± 5
Duration (years)	-	7.5 ± 4.4	-	-
Body weight (kg)	68 ± 11	79 ± 15	0.004	71 ± 14
Body mass index ($kg \cdot m^{-2}$)	24.2 ± 3.0	29.5 ± 5.0	0.008	24.3 ± 1.6
Fat-free mass (kg)	53 ± 11	52 ± 8	ns	54 ± 13
Fat mass (%)	24 ± 01	33 ± 9	0.03	26 ± 6
Waist (cm)	81 ± 8	96 ± 11	0.003	82 ± 10
Waist/hip ratio	0.82 ± 0.09	0.92 ± 0.06	0.009	0.79 ± 0.10
Systolic BP (mmHg)	114 ± 17	126 ± 15	0.08	115 ± 12
Diastolic BP (mmHg)	76 ± 11	84 ± 10	ns	75 ± 4
Heart rate (bpm)	67 ± 6	70 ± 11	ns	74 ± 12
HbA_{1c} (%)	5.4 ± 0.2	7.6 ± 0.6	<0.0001	5.1 ± 0.2
Fasting glucose (mmol/L)	4.8 ± 0.6	8.0 ± 1.3	<0.0001	4.5 ± 0.3
Fasting insulin (pmol/L)	41 [40]	75 [58]	0.002	20 [11]
Fasting Na^+ (mEq/L)	137 [3]	138 [2]	ns	136 [2]
Fasting K^+ (mEq/L)	4.7 [0.6]	4.7 [0.5]	ns	5.5 [0.8]
eGFR ($ml \cdot min^{-1} \cdot 1.73m^{-2}$)#	105 [21]	101 [17]	ns	114 [13]

* entries are mean±SD or median [interquartile range]; *Controls* are healthy subjects receiving the main protocol, *SGLT2i* are healthy subjects participating in the empagliflozin protocol.
° by unpaired *t* or Mann Whitney *U* test for T2D *vs* control.
calculated using the CKD-EPI formula (Levey AS, Inker LA. Assessment of Glomerular Filtration Rate in Health and Disease: A State of the Art Review. Clin Pharmacol Ther. 2017;102:405-419**).**

Supplemental Table 2 – Plasma glucose, insulin, sodium (Na^+), and potassium (K^+) concentrations, and whole-body glucose uptake (WBGU) in controls and patients with type 2 diabetes (T2D).*

	Controls		T2D		ANOVA		
	Saline	**Insulin**	**Saline**	**Insulin**	p^1	p^2	p^3
Mean plasma glucose (mmol/L)	22.0 ± 1.5	21.7 ± 0.9	21.7 ± 0.2	21.5 ± 0.5	ns	ns	ns
Mean plasma insulin (pmol/L)	55 [61]	712 [211][a]	44 [57]	690 [325][a]	ns	<0.0001	ns
Mean plasma Na^+ (mEq/L)	131 ± 2	132 ± 2	132 ± 1	132 ± 2	ns	ns	ns
Mean plasma K^+ (mEq/L)	5.0 ± 0.2	4.3 ± 0.1[a]	5.0 ± 0.4	4.4 ± 0.3[a]	ns	<0.0001	ns
WBGD ($\mu mol \cdot min^{-1} \cdot kg_{FFM}^{-1}$)	36 [16]	183 [48][a]	27 [11]	101 [48][a]	0.0004	-	0.0003

* entries are mean ± SD or median [IQR]; WBGD = whole-body glucose disposal; p^1 = group effect; p^2 = period effect; p^3 = interaction (group *x* period) by repeated measures ANOVA; [a] $p<0.001$; [b] $p<0.01$; [c] $p<0.05$ for the paired comparison between saline and insulin by Wilcoxon signed rank test in each group.

Supplemental Table 3 – Plasma glucose, insulin and whole body glucose disposal (WBGD) during the studies of the empagliflozin group.*

	Baseline	**Empa**	***p*^{1}**	**+Saline**	**+Insulin**	*p*^{2}
Mean plasma glucose (mmol/L)	4.5 ± 0.3	4.5 ± 0.2	ns	9.9 ± 0.5	9.4 ± 0.7	0.02
Mean plasma insulin (pmol/L)	20 [29]	7 [3]	0.02	28 [17]	649 [318]	0.02
Mean plasma Na^+ (mEq/L)	138 ± 1	137 ± 1	ns	137 ± 1	137 ± 1	ns
Mean plasma K^+ (mEq/L)	5.7 ± 0.6	5.1 ± 0.6	ns	4.9 ± 0.3	3.6 ± 0.1	0.02
WBGD ($\mu mol \cdot kg_{FFM}^{-1} \cdot min^{-1}$)	-	-	-	13.8 [1.6]	68.0 [20.0]	0.02

* entries are mean ± SD or median [IQR]; p^1 for empa period *vs* baseline; p^2 for the paired comparison between saline and insulin (Wilcoxon signed rank test).

Supplemental Table 4 – Fluid balance.*

	Controls	T2D	*p*	Empa
Glucose solution (mL)	2,757 [2,078]	2,581	ns	1,064 [340]
Saline (mL)	10 [375]	0 [125]	ns	400 [1,000]
Per os water (mL)	675 [800]	1,300 [875]	ns	800 [725]
Diuresis (mL)	2,950 [1,671]	2,684	ns	2,256 [535]
Overall fluid balance (mL)	+807 [981]	+1,104 [738]	ns	-24 [721]
Fluid balance (insulin – saline)	+1,194 [1,294]	+367 [740]	0.003	+547 [655]

* entries are median [interquartile range].