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Original Article

The effect of puerarin, as add-on therapy, on renal outcomes, oxidative stress and inflammatory cytokines in type 2 diabetic patients with hypertension

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Abstract: Co-occurrence of diabetes (DM) and hypertension increases the risk of renal complications. Inflammation and oxidative stress play roles in diabetic nephropathy (DN) and hypertensive nephropathy (HN). Puerarin, an ingredient isolated from *Radix Puerariae*, has been reported for its anti-inflammatory and anti-oxidative stress in some diseases. The major aims of this study were to detect the potential renoprotective effects of puerarin in type 2 diabetic patients with co-existed hypertension and its possible mechanisms. Eighty-three patients were divided into conventional therapy group (40 cases) and add-on therapy group (43 cases). In addition to conventional treatment, the add-on therapy group was given puerarin (p.o., 75 mg, bid) during the two years investigation. Fasting plasma glucose (FPG), HbA_{1c} and blood pressure were monitored. Renal damage were evaluated by measuring levels of urinary neutrophil gelatinase associated lipocalin (NGAL) and urinary kidney injury molecule-1 (KIM-1), serum creatinine, urinary albumin-to-creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR). The haemodynamics of the kidney were evaluated by color Doppler ultrasonography. Besides, some inflammatory mediators and oxidative stress markers that play roles in DN and HN were measured. The results showed that blood pressure and blood glucose were well-controlled in the two groups. Puerarin improved the renal outcomes, inhibited the productions of inflammatory mediators and suppressed the oxidative stress in the add-on therapy group if compared to the conventional therapy group. We conclude that puerarin as add-on therapy to conventional treatment has renoprotective effects in type 2 diabetic patients with co-existed hypertension.

Keywords: Puerarin, add-on therapy, renoprotective effects, oxidative stress, inflammatory cytokines, diabetes with co-existed hypertension

Introduction

Diabetes mellitus (DM) is a chronic disease with high prevalence [1]. According to the International Diabetes Federation, 7.8% of the world's population will have DM (of which more than 90% patients are known to have type 2 DM) by 2030. DM is frequently accompanied by disabling long-term vascular complications such as DN. Approximately 30% of the diabetic patients are affected by DN which is the leading cause of end-stage renal disease. In clinic, many type 2 diabetic patients also have co-existed hypertension. Hypertension is a well known disease that leads to renal vascular damage. And it has been proved that the co-occurrence of DM and hypertension leads to more complex pathophysiological changes and increases the risk of vascular events [2, 3]. Adequate management of blood glucose blood pressure, especially using angiotensin-converting enzyme (ACE) inhibitor and long-acting calcium channel blocker, can slow the progression of renal dysfunction. However, due to the complexity of the physiopathological mechanisms of DN and HN, the glycemic and hypotensive treatments seem not sufficient for these patients.

Although DN and HN have different pathogenesis, there is something in common in their pathogenic mechanisms. Numerous evidences from *in vitro* experiments, animal studies and clinical investigations have proved that DN is an

Table 1. Baseline clinical characteristics of the type 2 diabetic patients with hypertension

Characteristics	Conventional group	Add-on group	*P* value
Age (years)	53.6±15.6	51.2±16.8	0.504
Body mass index (kg/m^2)	25.07±5.10	24.51±5.38	0.628
SBP (mmHg)	125.32±8.14	123.11±6.43	0.176
DBP (mmHg)	81.75±5.86	80.91±4.81	0.478
FPG (mmol/L)	5.50±0.39	5.61±0.37	0.193
HbA_{1c} (%)	6.39±0.53	6.45±0.48	0.570
eGFR (ml/min/1.73 m^2)	75±10.07	77±11.80	0.482
UACR (μg/mg)	83.07±14.71	85.20±17.39	0.549
KIM-1 (pg/mL)	1868.55±350.30	1789.08±405.95	0.344
NGAL (ng/mL)	29.62±6.76	30.01±7.05	0.795
Creatinine (μmol/L)	82.10±19.14	86.18±21.38	0.364
RI	0.70±0.06	0.72±0.07	0.160
TNF-α (pg/mL)	13.08±3.26	14.11±3.80	0.188
IL-6 (pg/mL)	15.76±2.59	15.01±3.04	0.231
H-CRP (μg/mL)	3.68±0.69	3.80±0.63	0.385
VCAM-1 (ng/mL)	530.52±81.75	550.70±89.93	0.289
MCP-1 (pg/mL)	352.50±45.08	363.37±50.71	0.306
HO-1 (μmol/L)	92.05±20.18	88.96±18.60	0.470
Bilirubin (μmol/L)	8.63±1.64	8.01±1.85	0.108
GSH-Px (U/L)	119.10±19.05	123.06±22.21	0.389
T-AOC (U/mL)	3.49±0.67	3.66±0.64	0.260
U-8-OHdG (ng/mg creatinine)	9.74±1.75	10.33±2.39	0.198
MDA (nmmol/mL)	12.74±2.03	13.37±2.17	0.175

Data were expressed as mean ± SD. [a]*P* < 0.05 vs the conventional group.

inflammatory disorder [4]. Increased levels of some inflammatory mediators were found in serum, renal glomeruli and tubules in the DN subjects [5, 6]. In DN, the inflammatory mediators regulate inflammatory responses with the participation of different cytokine-associated signaling pathways [6]. The elevated inflammatory responses trigger complex reactions and lead to renal damage. Based on the role of inflammation in DN, anti-inflammatory strategies have been tested to treat DN [7]. Many agents possessing anti-inflammatory activities have recently exhibited renoprotective effects in animal models and patients with DN [8]. Similarly, hypertension is also regarded as an inflammatory state [9]. There now are convincing data that the hypertension-included inflammatory response, including the over-production of inflammatory mediators, contributes to the initiation and progression of HN [9, 10]. Anti-inflammatory therapies are also believed to be new therapeutic strategies for the treatment of HN [11].

The other common pathogenic mechanism for HN and DN is oxidative stress. Numerous studies have proved that diabetic individuals produced more reactive oxygen species (ROS) than the normal controls [12], which originate from the abnormal glucose and FFA metabolism through multiple pathways. The excessive ROS may induce endothelial dysfunction, mesangial expansion, thickening of glomerular and tubular basement membranes, inflammation and cell apoptosis. Administration of antioxidants has been shown to be effective in ameliorating DN [13]. Oxidative stress has also been shown to be increased in hypertension. And the enhanced oxidative stress is thought to be associated with the development of the renal complications of hypertension [14]. Atef ME found the enhanced oxidative stress in VSMC from spontaneously hypertensive rats contributed to the enhanced expression of Gqα/PLCβ1 proteins and the resultant VSMC hypertrophy [15]. There is evidence that oxidative stress determines podocyte apoptosis and generation of segmental glomerulosclerosis in hypertensive kidney damage [16]. Therefore, antioxidant therapy is an important aspect of the therapeutic strategy for HD [17, 18].

In addition, oxidative stress and inflammatory responses act synergistically in the pathogenesis of renal injury [19]. The reactive oxygen species can promote the production of inflammatory mediators, such as TNF-α, VCAM-1 and MCP-1, and inflammatory responses can enhance the oxidative stress [20]. Therefore, agents that have both anti-inflammatory and anti-oxidative activities seem to be appropriate choices for patients with diabetes and co-existed hypertension [21].

Puerarin is an ingredient isolated from *Radix Puerariae*. A large number of early studies have reported that puerarin has multiple activities including anti-inflammatory and anti-oxidative activities [22, 23]. It has been used to treat angina pectoris, myocardial infarction, tumor, neural regeneration, hyperlipidaemia and many other disorders [24]. In China, it has been tested to management DN in a few clinic studies, but little is known about its underlying mechanisms. A very recent study reported that puerarin attenuated early diabetic kidney injury through down-regulation of matrix metalloproteinase 9 in streptozotocin-induced diabetic rats [25]. A more recent study also found that puerarin improved early-stage renal damages and suppressed the expression of ICAM-1 and TNF-α in diabetic rats [26]. But to our knowledge, its effects on HN have not been studied to date. Moreover, no studies investigated its effects on type 2 diabetic patients with hypertension and its underlying mechanisms remains unclear.

Therefore, this study was conducted aiming to detect the possible renoprotective effects of puerarin as add-on therapy to conventional treatment in type 2 diabetic patients with hypertension and investigate its effects on some oxidative stress markers and inflammatory mediators which play a role in DN and HN.

Materials and methods

Participants and groups

A total of eighty-three type 2 diabetic patients with hypertension were included in the study. The baseline characteristics of the patients were evaluated and listed in **Table 1**. The patients were divided into two groups: conventional therapy group (conventional group) (40 cases) and add-on therapy group (add-on group) (43 cases). The inclusion criteria in this study were: (i) between the ages of 20-70 years with type 2 DM and hypertension; (ii) with adequately controlled blood glucose ($HbA_{1c} \leq$ 7.0%, fasting plasma glucose < 6.1 mmol/L) and adequately controlled blood pressure (systolic pressure < less than 140 mmHg and diastolic blood pressure < less than 90 mmHg) under lifestyle modification and administration of hypotensive and hypoglycemic agents; (iii) using calcium channel blockers and ACE inhibitors as hypotensive agents, and using metformin and gliclazide as hypoglycemic agents; (iv) UACR between 30 μg/mg and 200 μg/mg. The following patients were excluded: (i) patients with any other types of diabetes; (ii) patients with any other diseases that might damage the renal function; (iii) patients with mental disease who might not follow the doctors' administration; (iv) patients with severe liver dysfunction; (v) patients with any serious or unstable disorders that might increase the withdrawal from this study; (vi) patients who were judged as being inappropriate by the physicians due to some other reasons. Informed consent was obtained from each patient. All the protocols were approved by the Ethics Committee of Maternal and Child Health Care Hospital of Zaozhuang.

Drug management

Since calcium channel blockers and ACE inhibitors are effective on DN and HN, all the patients from the two groups received benazepril and amlodipine as hypotensive agents. All the patients from the two groups received metformin and gliclazide as hypoglycemic agents. In addition to the hypotensive and hypoglycemic agents, patients in the add-on group were given puerarin (p.o., 75 mg, bid). The management lasted for 2 years.

Fasting plasma glucose and HbA_{1c}

Blood samples were collected after overnight fasting. Serum levels of FPG were measured by an automatic biochemistry analyzer. Serum levels of HbA_{1c} were measured using high-performance liquid chromatography (Tosoh Corp., Tokyo, Japan).

Blood pressure

Blood pressure was measured on the morning by well-trained physicians using mercury sphygmomanometer.

Renal damage markers

Levels of urinary NGAL and KIM-1 were assessed by ELISA kits (R&D Systems, Inc., Minneapolis, MN, USA). Urinary albumin concentrations were measured using turbidimetric immunoassay kits (Wako Pure Chemical In-

Table 2. Levels of blood pressure and blood glucose of the patients after treatment

	Conventional group	Add-on group	*P* value
FPG (mmol/L)	5.62±0.79	5.80±0.53	0.222
HbA_{1c} (%)	6.70±0.88	6.60±0.61	0.536
SBP (mmHg)	130.11±9.06	127.91±11.20	0.328
DBP (mmHg)	83.51±5.63	84.02±7.34	0.718

Data were expressed as mean ± SD. [a]*P* < 0.05 vs the conventional group.

Table 3. Changes of renal outcomes from the baseline to the end in the patients

	Conventional group	Add-on group	*P* value
eGFR (mL/min/1.73 m^2)	-4.31±1.53	5.26±2.09[a]	0.000
UACR (μg/mg)	30.62±6.70	-13.28±3.01[a]	0.000
KIM-1 (pg/mL)	355.69±50.52	-248.39±41.67[a]	0.000
NGAL (ng/mL)	7.43±1.55	-5.82±1.43[a]	0.000
Creatinine (mmol/L)	5.25±1.36	-4.50±1.60[a]	0.000
RI	0.02±0.01	-0.06±0.02[a]	0.000

Data were expressed as mean ± SD. [a]*P* < 0.05 vs the conventional group.

Table 4. Changes of inflammatory mediators from the baseline to the end in the patients

	Conventional group	Add-on group	*P* value
TNF-α (pg/mL)	3.57±0.96	-2.76±0.83[a]	0.000
IL-6 (pg/mL)	2.70±0.57	-2.09±0.61[a]	0.000
H-CRP (μg/mL)	0.53±0.17	-0.43±0.09[a]	0.000
VCAM-1 (ng/mL)	80.14±13.00	-109.30±30.52[a]	0.000
MCP-1 (pg/mL)	43.08±9.18	-31.07±6.44[a]	0.000

Data were expressed as mean ± SD. [a]*P* < 0.05 vs the conventional group.

Table 5. Changes of ant-oxidative/oxidative stress markers from the baseline to the end in the patients

	Conventional group	Add-on group	*P* value
HO-1 (μmol/L)	-5.26±1.40	7.61±1.39[a]	0.000
Bilirubin (μmol/L)	-1.38±0.26	2.17±0.51[a]	0.000
GSH-Px (U/L)	-5.20±1.26	18.30±4.04[a]	0.000
T-AOC (U/mL)	-0.30±0.06	0.51±0.11[a]	0.000
U-8-OHdG (ng/mg creatinine)	1.05±0.22	-1.93±0.50[a]	0.000
MDA (nmmol/mL)	0.86±0.19	-1.94±0.34[a]	0.000

Data were expressed as mean ± SD. [a]*P* < 0.05 vs the conventional group.

dustries, Ltd., Osaka, Japan). Creatinine concentrations in urine and serum were determined by automatic biochemistry analyzer. UACR was calculated as urinary albumin concentration divided by creatinine concentration. The eGFR was calculated using the Cockroft-Gault formula: (140-age) × body weight/72 × serum creatinine, and × 0.85 for female patients. The eGFR was expressed in ml/min/1.73 m^2.

Ultra sonographic measurement

The peak systolic velocity (PSV) and the end diastolic velocity (EDV) of interlobar renal artery were measured to evaluate the haemodynamics of the kidney using color Doppler ultrasonography. The renal arterial resistance index (RI) was calculated using the following formula: (PSV-EDV)/PSV.

Inflammatory mediators

Serum levels of TNF-α, IL-6, high-sensitivity C-reactive protein (Hs-CRP), vascular cell adhesion molecule 1 (VCAM-1) and monocyte chemoattractant protein (MCP)-1 were assessed using ELISA kits (R&D Systems, Inc., Minneapolis, MN, USA; Cusabio Company, Wuhan, China).

Oxidative stress markers

Levels of heme oxygenase-1 (HO-1), bilirubin, glutathione peroxidase (GSH-Px), total antioxidant capacity (T-AOC) and malondialdehyde (MDA) in serum were measured using commercially available kits (Nanjing Jiancheng Company, Nanjing, China). Levels of urinary 8-hydroxy-deoxyguanosine (U-8-OHdG) were measured by ELISA (Biodee Biotechnology Company, Beijing, China).

Statistical analysis

All data were analyzed by SPSS 11.5 statistical software (SPSS, Inc., Chicago, IL, USA). Data are expressed as mean ± standard deviation (mean ± SD), differences were evaluated by *t*-test.

Results

Clinical characteristics before treatment

Table 1 showed the baseline clinical characteristics of the patients. All the baseline clinical characteristics of the conventional therapy group and the add-on group were comparable ($P>0.05$). The original and individual data for **Table 1** are shown in Supplementary Table 1.

Levels of blood glucose and blood pressure after treatment

As shown in **Table 2**, both the blood glucose and the blood pressure of the two groups were well controlled. No significant differences were observed between the two groups ($P>0.05$). The original and individual data for **Table 2** are shown in Supplementary Table 2.

Changes of renal outcomes after treatment

The add-on therapy group showed significant decreases in levels of UACR (-13.28 versus 30.62 μg/mg), urinary KIM-1 (-248.39 versus 355.69 pg/mL), urinary NGAL (-5.82 versus 7.43 ng/mL) and serum creatinine (-4.50 versus 5.25 mmol/L), but a significant increase in eGFR (5.26 versus -4.31 mL/min/1.73 m^2), if compared to the conventional group, suggesting puerarin improved the renal function of the patients with diabetes and hypertension. The ultrasonographic measurement showed marked elevations in EDV (2.10 versus -0.63 cm/sec) and PSV (5.33 versus -1.51 cm/sec), but a marked reduction in RI (-0.06 versus 0.02) in the add-on group if compared to the conventional group, suggesting that puerarin improved the renal haemodynamics of the patients. (Shown in **Table 3**). The original and individual data for **Table 3** are shown in Supplementary Table 3.

Changes of inflammatory mediators after treatment

We measured levels of some inflammatory mediators that play a role in DN and HN. We found add-on therapy induced significant decreases in levels of TNF-α (-2.76 versus 3.57 pg/mL), IL-6 (-2.09 versus 2.70 pg/mL), Hs-CRP (-0.43 versus 0.53 μg/mL), VCAM-1 (-109.30 versus 80.14 ng/mL) and MCP-1 (-31.07 versus 43.08 pg/mL) if compared to the conventional group, suggesting that puerarin could inhibit the productions of these inflammatory mediators in the patients with diabetes and hypertension. (Shown in **Table 4**). The original and individual data for **Table 4** are shown in Supplementary Table 4.

Changes of oxidative stress and anti-oxidative stress markers after treatment

Excessive oxidative stress can exacerbate DN and HN. We measured levels of some oxidative stress and anti-oxidative stress markers to evaluate the oxidative state of the patients. The results showed there were significant reductions in levels of MDA (-1.94 versus 0.86 nmmol/mL) and U-8-OHdG (-1.93 versus 1.05 ng/mg creatinine), as well as significant elevations in levels of HO-1 (7.61 versus -5.26 μmol/L), bilirubin (2.17 versus -1.38 μmol/L), GSH-Px (18.30 versus -5.20 U/L) and T-AOC (0.51 versus -0.30 U/mL) in the add-on group compared to the conventional group, suggesting that puerarin improved the anti-oxidative activity and inhibited the oxidative activity of the patients with diabetes and hypertension. (Shown in **Table 5**). The original and individual data for **Table 5** are shown in Supplementary Table 5.

Discussion

In the current clinical investigations, we for the first time reported that puerarin as add-on therapy to conventional treatment slowed the progression of renal damage in type 2 diabetic patients with hypertension, and suppressed the expression of oxidative stress markers and inflammatory mediators.

In clinic, lots of patients have type 2 DM and co-existed hypertension. The co-occurrence of DM and hypertension leads to more complex pathophysiological changes and increases the risk of renal damage [2, 3]. Although with well-controlled blood glucose blood pressure, the renal function may still get worse with the extension of the disease course [21]. More drugs targeting at the various pathogenic mechanisms seem necessary for such patients. In the current study, we administrated puerarin, an ingredient isolated from *Radix Puerariae*, to type 2 diabetic patients with hypertension whose baseline UACR was between 30 μg/mg and 200 μg/mg. Before enrolled to this study, the patients had well-controlled blood glucose and blood pressure by using calcium channel blockers, ACE inhibitors, metformin and gliclazide for at least 1 years. After the 2 years' observation in our study, we found both the

conventional group and the add-on group had well-controlled blood glucose blood pressure. We evaluated the renal outcomes of the patients. We found marked decreases in levels of serum creatinine, UACR, urinary KIM-1 and urinary NGAL, but an increase in eGFR in the add-on group, if compared to the conventional group. Urinary KIM-1 and urinary NGAL have recently been regarded as urinary biomarkers for early diabetic nephropathy in type 2 diabetic patients in literature [27, 28]. Besides the laboratory examinations, the ultra-sonographic measurement showed that the add-on therapy significantly increased PSV and EDV, but decreased RI if compared to the conventional therapy group, which suggested that puerarin improved the renal haemodynamics. All the data of the renal outcomes indicated that the add-on therapy exhibited renoprotective effects in the patients with type 2 DM and co-existed hypertension.

Inflammation plays an important role in DN and HN [4-6, 9, 10]. In order to detect the possible mechanisms by which puerarin exerted its renoprotective effects, we investigated levels of some inflammatory mediators that are involved in HN and DN. TNF-*α and* IL-6 are well known pro-inflammatory cytokines that promote the development and progression of HN and DN by inducing renal inflammation, endothelial damage, mesangial expansion, glomerular thickening and renal cell apoptosis. Animal and clinical studies have well demonstrated that suppressing their over-production could attenuate the renal damage in DN and HN [29, 30]. VCAM-1 and H-CRP are also inflammatory mediators that are associated with the vascular complications of DM and hypertension. They have been recently regarded as new potential therapeutic targets for DN and HN [21]. MCP-1 can induce the macrophage infiltration into glomeruli and macrophage infiltration is associated with renal injury. Increased levels of MCP-1 were found in DN and HN [31, 32]. It has been proved that urinary MCP-1 excretion is positively correlated with diabetic glomerular injury and urinary MCP-1 is regarded as a marker to evaluate renal damage induced by diabetes and hypertension [32]. Furthermore, studies showed that MCP-1 null mice were protected against DN and blockade of the MCP-1 signaling could ameliorate the glomerulosclerosis of diabetic subjects. In our study, we measured the levels of these inflammatory mediators. We found the add-on therapy induced significant reductions in levels of TNF-*α,* IL-6, VCAM-1, Hs-CRP and MCP-1 if compared to the conventional group. The results were partially consistent with a recent study that reported puerarin improved early-stage renal damages and suppressed the expression of ICAM-1 and TNF-α in diabetic animals [26]. In addition, the anti-inflammatory effects of puerarin in the patients with type 2 DM and co-existed hypertension were consistent with studies that reported the amelioration of inflammation by puerarin in other diseases [23, 33]. Based on the role of these inflammatory mediators in DN and HN, we supposed that the reductions in their levels should be beneficial for the amelioration of the renal damage in the patients with type 2 DM and co-existed hypertension.

Numerous studies clearly demonstrated that both diabetic and hypertensive state produced oxidative stress [12, 14, 17, 18]. And oxidative stress plays an important role in HN and DN by damaging endothelial cells, promoting glomerulosclerosis, inducing cell apoptosis, and some other mechanisms. 8-OHdG and MDA are well-known oxidative stress markers that are associated with HN and DN. Agents that could inhibit 8-OHdG and MDA exhibited ameliorative effects on renal damage [21, 34, 35]. Heme oxygenase (HO) plays a critical role in attenuating the production of reactive oxygen species through inducing the production of carbon monoxide and biliverdin/bilirubin and the release of free iron. Bilirubin possesses potent antioxidant properties. Bilirubin treatment was recently shown to improve urine output, glomerular filtration rate, tubular function, and mitochondrial integrity after in rats with ischemia/reperfusion injury [36] which is associated with oxidative stress. Hemin, a strong HO-1 (inducible form of HO) inducer, has been proved to ameliorate renal function and decrease oxidative stress in rats with renal ischemia/reperfusion injury [37]. However, decreased HO-1 expression and decreased HO activity were found in DM [38]. And up-regulation of HO-1 ameliorated diabetic vascular dysfunction and inhibited the expression of cytokines TNF, IL-1 and IL-6 [39]. Those findings suggested the protective role of HO-1 in renal damage. Besides, Heme oxygenase-1 has been recently regarded as a novel target for the treatment of other diabetic complications [40]. In the current clinical study, we found puerarin induced significant increases in levels of HO-1, bilirubin and T-AOC, but marked reductions in levels of U-8-OHdG

and MDA in the add-on group if compared to the conventional group. The finding indicated that puerarin improved the anti-oxidative activity and inhibited the oxidative stress in the patients with type 2 DM and co-existed hypertension. The attenuation of the oxidative stress by puerarin should contribute to the renoprotective effects we observed in the patients. Besides our finding, previous studies also reported the anti-oxidative activity of puerarin in some other diseases [22, 41].

Thus, with well-controlled blood glucose and blood pressure by using calcium channel blocker, ACE inhibitor, metformin and gliclazide as hypotensive and hypoglycemic agents, the renal dysfunction of the type 2 diabetic patients with hypertension still progressed during the two years' observation. However, the add-on therapy with puerarin to the conventional treatment attenuated the oxidative stress and inhibited the productions of some inflammatory mediators that play roles in DN an HN. Accompanied by the suppression of oxidative stress and inflammatory mediators, the renal dysfunction of the patients was ameliorated. Therefore, puerarin might be a potential drug as add-on therapy in the management of renal damage in patients with type 2 DM and co-existed hypertension who cannot achieve desired effects from conventional treatment.

Disclosure of conflict of interest

None.

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Supplementary Table 1. Original and individual data for **Table 1** in the manuscript

	Age (years)	Body mass index (kg/m^2)	SBP (mmHg)	DBP (mmHg)	FPG (mmol/L)	HbA_{1c} (%)	eGFR (ml/min/1.73 m^2)	UACR (μg/mg)	KIM-1 (pg/mL)	NGAL (ng/mL)	Creatinine (μmol/L)	RI	TNF-α (pg/mL)	IL-6 (pg/mL)	H-CRP (μg/mL)	VCAM-1 (ng/mL)	MCP-1 (pg/mL)	HO-1 (μmol/L)	Bilirubin (μmol/L)	GSH-Px (U/L)	T-AOC (U/mL)	U-8-OHdG (ng/mg creatinine)	MDA (nmmol/mL)
Patient No. 1 in conventional group	36	27.94	129	88	5.4	6.05	91.31	55.62	1490.32	20.15	66.31	0.66	8.36	12.6	3.26	401.8	289.31	125.29	12.95	152.36	4.42	7.57	9.9
Patient No. 2 in conventional group	27	28.5	116	87	5	6.15	86.06	70.23	1646.7	25.65	80.24	0.73	11.09	14.09	3.36	484.5	322.3	105.21	9.52	138.02	4.23	8.25	12.46
Patient No. 3 in conventional group	53	19.73	121	88	6	6.99	60.32	98.45	2104.1	39.31	80.25	0.75	14.16	20.15	3.79	610.47	398.62	76.79	7.59	96.32	2.67	10.79	14.71
Patient No. 4 in conventional group	66	27.89	117	80	5.9	6.96	58.32	100.53	2134.1	41.65	110.64	0.81	17.24	19.91	5.07	657.21	423.03	70.35	7.26	90.44	2.32	13.42	14.62
Patient No. 5 in conventional group	56	29.09	115	75	5.5	6.87	83	85.35	1984.67	29.87	69.42	0.72	12.96	16.22	3.39	510.28	345.83	97.3	7.48	109.72	3.3	9.35	12.74
Patient No. 6 in conventional group	59	17.86	127	75	5.6	6.85	62.45	98.23	1987.09	40.1	107.3	0.77	15.63	18.03	3.9	607.31	424.08	73.19	6.29	90.94	2.91	9.4	14.52
Patient No. 7 in conventional group	43	23.4	122	81	5.3	6.12	76.15	74.2	1765.23	23.1	68.31	0.62	11.66	13.8	3.3	510.59	316.66	90.48	9.01	130.15	4.19	8.84	12.25
Patient No. 8 in conventional group	26	18.38	137	83	5	5.6	90.42	67	1510.35	22	70.08	0.64	8.43	13.31	3.16	438.19	281.17	129.34	11.54	143.8	4.23	7.87	10.47
Patient No. 9 in conventional group	28	24.01	129	74	5.3	6.09	91.37	68.2	1569.99	23.35	61.46	0.61	9.17	13.83	3.19	451.33	322.41	120.09	11.81	145.62	4.01	8.31	11.9
Patient No. 10 in conventional group	56	26.41	131	75	5.9	7	65.03	105.5	2409.5	39.79	110.57	0.8	16.75	20.33	4.72	651.9	431.14	63.22	6.55	88.02	2.47	12.32	15.53
Patient No. 11 in conventional group	58	35.39	135	77	5.8	7	63.12	106.32	2465.91	39.51	111.35	0.79	17.41	19.48	4.52	657.13	418.3	66.1	7.03	98.78	2.39	13.2	16.5
Patient No. 12 in conventional group	65	27.42	116	86	5	6.34	86.21	70.25	1368.7	22.5	74.32	0.65	12.53	14.36	3.05	478.01	327.54	116.3	10.64	132.7	4.09	9.42	10.88
Patient No. 13 in conventional group	62	19.1	118	88	5.1	6.43	80.5	75.23	1468.13	28.7	67.09	0.61	9.77	14.77	3.05	482.6	308.2	96.25	8.49	131.31	4.1	8.99	12.2
Patient No. 14 in conventional group	60	18.37	117	75	5.1	6.1	93.31	66.1	1379	25.51	75.46	0.63	9.26	12.9	3.16	418.64	301.62	120.79	12.66	142.69	4.36	7.6	11.42
Patient No. 15 in conventional group	70	16.46	122	89	5.2	6.04	75.33	78.3	1557.03	25.44	69.43	0.64	8.95	14.89	3.26	468.32	342.9	109.4	9.38	135.66	3.86	8.09	12.8

Patient No. 16 in conventional group	70	17.45	138	88	5.2	6.23	77.05	86.3	2047.5	34.4	81.23	0.74	13.9	14.2	3.53	538.85	337.31	90.31	8.27	120.09	3.31	10.1	12.66
Patient No. 17 in conventional group	24	16.25	130	78	5.1	5.6	93.21	66.12	1678.21	23.87	59.13	0.67	9.14	13	3.16	408.5	287.08	128.9	9.9	141.72	4.4	7.15	11.27
Patient No. 18 in conventional group	67	17.62	115	89	6.1	6.98	68.93	97.4	2295.25	36.33	111.96	0.78	15.5	19.04	3.99	602.93	389.66	66.5	7.3	93.73	2.71	11.26	14.83
Patient No. 19 in conventional group	63	24.82	135	74	6	5.5	73.6	78.31	1571.97	22.83	65.32	0.69	14.21	13.3	3.41	530.74	326.97	101.4	8.35	130.5	3.73	9.41	12.88
Patient No. 20 in conventional group	56	36.45	138	78	5.4	5.8	70.12	79.56	1657.37	21.51	75.54	0.67	10.44	14.28	3.28	518.64	326.84	86.34	8.11	123.53	3.58	8.69	11.99
Patient No. 21 in conventional group	56	29.4	136	78	5.3	6	75.88	85.33	1902.41	30.8	62.11	0.72	13.76	14.43	3.47	538.31	333.79	87.71	8.02	111.38	3.35	9.03	12.81
Patient No. 22 in conventional group	66	30.44	139	89	6	7	57.13	115.32	2571.93	40.02	124.09	0.82	19.5	21.26	5.38	682.08	430.8	57.36	6.12	88.35	2.29	13.7	16.65
Patient No. 23 in conventional group	44	27.32	117	88	5	6.8	69.73	88.3	1703.45	28.25	80	0.7	14.65	17.24	3.33	527.36	368.86	80.5	8.13	109.55	3.42	11.1	13.62
Patient No. 24 in conventional group	68	30.62	115	75	6	6.65	80.1	66	2481.59	22.9	71.1	0.69	9.36	12.3	2.99	439.05	316.95	121.49	10.2	135.2	4.18	7.23	9.4
Patient No. 25 in conventional group	64	31	118	87	5.3	5.55	80.36	53.2	1467.9	24.85	55.14	0.61	8.91	12.86	2.8	422	299.44	122.08	10.3	147.11	4.53	7.76	10.76
Patient No. 26 in conventional group	68	25.75	122	76	6	7	70.3	85.36	1865.32	31.82	70.32	0.72	13.2	14.25	3.26	536.9	346.8	90.22	7.99	124.65	3.2	10.84	12.96
Patient No. 27 in conventional group	29	26.36	122	89	5.2	5.76	90.5	72.9	1635.96	20.8	65.19	0.69	10.04	13.71	3.35	456.35	320	92.7	9.01	122.99	3.69	9.1	10.88
Patient No. 28 in conventional group	33	21.67	120	75	6	6.83	68.27	84.2	2042.8	26.35	70.35	0.72	15.1	17.32	3.29	521.97	342.8	88.31	8.22	116.47	3.32	10.59	12.25
Patient No. 29 in conventional group	68	16.14	129	86	5.3	6.1	78	76.37	1461.78	24.66	67.2	0.7	9.22	13.84	3.18	435.2	326.37	92.02	9.12	125.75	4.08	8.46	10.49
Patient No. 30 in conventional group	56	27.35	136	88	6	6.73	68.9	99.65	2209.57	32.27	101.3	0.75	16.64	17.79	4.6	633.3	413.57	62.99	7.64	97.26	2.63	11.9	14.77
Patient No. 31 in conventional group	62	28.32	139	77	5.3	6.8	68.3	92.5	1902.37	36.85	93.06	0.75	16.03	18.44	4.94	625.7	405.87	71.2	7.68	100.7	3.04	9.83	13.27
Patient No. 32 in conventional group	30	25.22	126	75	5.2	5.6	80.27	77.56	1684.26	25.67	66.38	0.68	10.5	13.06	3.38	512.9	329.65	98.14	8.5	131.08	3.91	9.68	11.14

Patient No. 33 in conventional group	63	27.36	138	86	5.1	5.59	80.36	72.5	1570.66	26.43	80.55	0.65	9.58	13.66	3.2	469.4	325.11	106.25	9.61	140.42	3.82	8.52	10.56
Patient No. 34 in conventional group	68	26.36	116	74	5.2	5.8	77.4	80.3	1855.81	30.22	81.32	0.71	15	16.3	3.58	531.9	346.7	90.09	8.13	120.88	3.56	9.91	11.52
Patient No. 35 in conventional group	69	24.21	121	88	6	6.98	61.87	109.9	2409.55	44.2	116.3	0.76	18.39	19.07	4.84	644.67	416.85	68.63	6.85	93.5	2.34	12.31	15.6
Patient No. 36 in conventional group	26	28.32	120	86	5.3	6.4	78.21	78.53	1672.4	23.16	68.88	0.66	13.54	14.5	3.37	462.4	322.86	93.28	8.69	130.57	3.8	9.17	8.55
Patient No. 37 in conventional group	63	26.46	122	81	6	6.93	66.57	90.7	2106.15	33.34	111.37	0.76	16.75	16	5.04	639.14	387.45	80.73	7.66	108.43	2.86	9.43	15.06
Patient No. 38 in conventional group	64	26.82	120	89	6	6.88	70.25	80.31	1672.22	30.7	91.22	0.63	14.06	15.4	3.44	521.6	365.06	86.4	8.82	115.51	3.77	9.8	13.41
Patient No. 39 in conventional group	69	25.13	123	80	5.1	6.4	81.53	85.2	1890.68	30.16	80.15	0.65	13.98	17.57	3.5	543	358.32	90.32	8.03	113.33	3.64	8.63	12.55
Patient No. 40 in conventional group	33	25.87	126	75	5.8	7	68.9	101.4	2543.96	35.65	112.66	0.78	18.3	19.1	4.6	649.71	421.8	67.89	6.44	94.92	2.99	12.56	16.73
Patient No. 1 in add-on group patient	23	25.23	125	75	6	6.62	75.33	95	2087.2	32.24	112.9	0.78	17.36	17.3	4.63	631.3	405.26	83.17	6.73	102.52	2.86	10.88	14.25
Patient No. 2 in add-on group patient	25	28.2	117	87	5.6	6.3	85.04	65.68	1360	23.18	78.26	0.68	10.02	11.73	3.4	410.53	296.37	110.39	10.02	158.37	4.61	7.92	9.42
Patient No. 3 in add-on group patient	24	21.86	137	77	5.6	6.06	96.83	53.87	1147.87	21.91	68.13	0.61	9.67	10.99	3.11	395.46	289.53	120.04	12.82	158.53	4.65	6.97	8.78
Patient No. 4 in add-on group patient	68	23.54	116	89	6.1	7	67.98	103.8	2198.8	41.48	121.47	0.82	17.11	18.48	4.35	654.83	431.66	65.3	5.07	94.22	2.96	12.32	15.71
Patient No. 5 in add-on group patient	54	19.36	120	80	4.9	5.4	67.8	81.8	1656	27.32	76.33	0.74	11.69	13.05	3.53	536.24	358.9	87.49	8.25	136.3	3.72	10.41	12.97
Patient No. 6 in add-on group patient	69	22.22	119	76	6	6.8	65.58	92.63	1797.53	34.79	88.5	0.8	17.2	16.32	4.16	616.7	389.42	71	7.03	108.32	3.16	11.07	13.96
Patient No. 7 in add-on group patient	37	24.6	122	80	5.4	6.3	96	52.25	1259.5	19.45	63.21	0.62	8.75	10.68	3.04	387.48	280.47	121.22	10.11	160.09	4.62	7.2	9.03
Patient No. 8 in add-on group patient	63	22	126	89	6	6.74	68.2	109.76	2529.12	38.61	124.23	0.84	19.03	18.75	4.61	624.6	425.8	65.06	6.88	98.77	2.89	12.65	16.8
Patient No. 9 in add-on group patient	33	24.3	117	77	5.6	5.8	90.3	60.62	1278.8	23.62	70.35	0.63	9.2	10.52	3.11	435.61	306.74	117.42	10.62	149.32	4.43	7.51	9.48

Patient No. 10 in add-on group patient	66	32.6	118	83	5.2	5.9	92.1	70.03	1607.3	23.59	68.82	0.64	10.77	12.06	3.35	458.65	327.84	96.55	8.02	140.32	4.29	8.67	12.57
Patient No. 11 in add-on group patient	25	30.2	139	89	5.3	6.15	82.6	70.98	1627.97	25.14	64.9	0.69	9.03	10.3	3.28	458.27	321.06	102.39	9.2	147.4	3.96	7.43	12.62
Patient No. 12 in add-on group patient	40	27.32	138	87	5.7	6	71.58	82.09	1854.26	26.96	75.13	0.71	12.58	13.04	3.45	542.85	359.77	90.44	7.96	136.5	3.89	10.6	13.85
Patient No. 13 in add-on group patient	69	18.55	124	88	5.9	7	64.7	95.75	2097.8	32.64	89.38	0.79	16.75	17.38	4.5	626.8	398.53	73.57	6.61	104.01	3.24	11.9	14.38
Patient No. 14 in add-on group patient	26	28.3	127	74	5.4	6.23	75.58	91.5	2187.2	36.31	100.8	0.8	15.8	17.69	4.48	638.5	401.69	80.36	7.28	105.36	3.21	11.88	14.69
Patient No. 15 in add-on group patient	70	26	121	86	5.9	6.9	66.7	107.4	2549.1	41.84	111.16	0.83	19.08	17.15	5	648	425.88	59.94	6.07	88.32	2.85	14.27	16.27
Patient No. 16 in add-on group patient	20	33.29	118	78	5.2	6.32	76.2	88.65	1984	30.26	70.86	0.72	16.15	14.88	3.26	621.43	371.9	80.76	7.17	127.47	3.69	10.91	13.48
Patient No. 17 in add-on group patient	59	26.31	133	75	5.5	5.89	83.31	82.9	1652.9	26.1	83.01	0.72	13.7	13.2	3.47	528.22	378.52	90.55	7.65	135.53	3.88	10.53	13.82
Patient No. 18 in add-on group patient	57	25.38	124	80	5.2	5.69	80.02	70.8	1352.46	22.82	68.13	0.68	10.62	13.68	3.23	501.86	316.22	90	9.48	137.08	4.33	8.5	11.58
Patient No. 19 in add-on group patient	66	18.54	131	81	6	6.9	68	107.53	2361.37	40.13	125.1	0.83	19.5	18.42	4.65	670.17	432.45	62.04	5.58	99.43	2.88	12.38	12.95
Patient No. 20 in add-on group patient	43	26.2	121	79	5.8	6.93	64.13	116.67	2482.11	46.19	109.04	0.82	20	20.3	4.8	662.51	437.62	65.46	5.21	88.59	2.59	15.31	16.83
Patient No. 21 in add-on group patient	62	18.3	121	80	4.9	6.35	69.11	96.12	1906.58	32.69	103.5	0.8	18.52	17.08	4.52	620.73	393.5	74.9	7.13	103.35	3.04	11.93	14.62
Patient No. 22 in add-on group patient	67	30.28	123	79	5.5	5.77	78.56	75.53	1362.66	26.7	65	0.65	10.65	11.68	3.3	505.9	325.85	100.37	9.25	144.42	3.96	8.63	12.07
Patient No. 23 in add-on group patient	69	17.11	117	77	6	6.82	70.31	91.9	2085.35	35.19	97.25	0.77	14.33	17.98	4.25	627.3	296.48	79.74	7.15	110.33	3.27	11.27	14.5
Patient No. 24 in add-on group patient	49	28.32	124	78	5.3	6.41	100.7	66.51	1268.44	20.18	60.4	0.65	10.36	11.41	3.16	450.83	321.69	114.09	9.01	144.96	4.31	6.96	11.48
Patient No. 25 in add-on group patient	45	16.52	120	80	4.8	5.89	107	65.94	1257.83	20.6	65.1	0.62	9.54	10.95	3.06	402.98	310.15	120.93	11.79	152.36	4.57	7.68	10.73
Patient No. 26 in add-on group patient	66	23.21	124	89	5.9	7	70.1	98.41	2155.84	33.7	103.28	0.75	17.2	18.4	4.4	584.66	405.38	86.31	5.88	99.01	3.1	11.65	14.57

Patient No. 27 in add-on group patient	27	20.04	127	85	6	6.86	91	55.87	1257.55	21.85	61.32	0.59	9.38	11.26	3.17	414.2	295.2	123.66	10.34	152.3	4.65	6.49	8.89
Patient No. 28 in add-on group patient	64	36	135	84	5.4	5.66	80.7	66.46	1363.9	24.74	60.52	0.64	9.79	12.6	3.3	427.12	309.53	109.35	10.11	146.22	4.38	7.92	11.63
Patient No. 29 in add-on group patient	70	19.65	124	75	5.9	6.86	76.36	81.38	1905.77	26.04	73.08	0.73	9.17	14.67	3.44	565.83	348.35	90.42	9.14	129.55	3.84	9.68	12.71
Patient No. 30 in add-on group patient	57	21.55	120	80	5.9	6.9	95.08	75.08	1348.03	27.33	63.19	0.66	11.84	15.37	3.48	525.27	320.08	98.8	9.89	130	4.4	8.72	12.85
Patient No. 31 in add-on group patient	50	17.32	115	76	5.9	6.7	65.58	94.22	1977.32	32.36	80.61	0.71	18.19	17.89	4.2	633.79	426.66	81.31	5.37	105.3	3.15	11.41	14.63
Patient No. 32 in add-on group patient	67	19.35	114	86	6	6.86	65.5	89	1652.96	31.83	76.15	0.74	16.05	15.5	3.55	588.44	402.73	92.08	7.72	125.42	3.42	11.8	14.61
Patient No. 33 in add-on group patient	33	22.66	127	85	5.6	6.9	65.99	105.88	2131.64	36.7	122.31	0.79	18.6	19.15	4.4	649.52	438.15	64.33	6.53	97.56	2.88	14.43	15.89
Patient No. 34 in add-on group patient	66	23.42	120	76	5.2	5.74	82.52	85.2	1592.11	27.27	67.3	0.7	14.48	14.3	3.34	531.8	370.31	89.35	7.13	129.74	3.73	10.5	13.51
Patient No. 35 in add-on group patient	62	27.5	116	81	5.7	7	65	117.8	2351.32	41.8	126	0.82	20.16	20.07	5.01	655.35	428.99	65.29	7.73	89.88	2.71	16.31	15.92
Patient No. 36 in add-on group patient	58	32.63	119	85	5.3	6.37	65.36	86.9	1909.55	24.2	74.9	0.75	13.47	14.58	3.26	526.6	350.61	90.4	7.55	127.26	3.61	9.95	13.64
Patient No. 37 in add-on group patient	30	16.12	120	75	6	6.95	68.9	99.5	1951.67	32.33	102	0.78	19.16	17.93	4.18	614.83	416.84	69.53	5.97	98.25	3.14	11.75	15.28
Patient No. 38 in add-on group patient	68	32.08	125	89	5.4	6.6	80.18	79.2	1436.08	24.91	82.2	0.66	12.55	12.6	3.25	503.09	351.74	90.86	8.14	123	4.1	9.47	13.62
Patient No. 39 in add-on group patient	28	19.65	121	76	5	6.38	95.65	63.85	1241.64	23.66	63	0.6	10.07	12.53	3.02	435.98	288.53	115.9	10.68	139.64	4.36	7.3	11.74
Patient No. 40 in add-on group patient	62	34.51	133	78	5.9	7	65.8	109.32	2097.33	43.09	114.66	0.8	18.01	18.5	4.51	673.7	418.64	67.04	6.19	98.32	2.99	11.52	15.77
Patient No. 41 in add-on group patient	60	27.97	116	79	6	6.85	65.14	100.93	2275.92	35.57	113.39	0.81	17.02	18.52	4.34	629.61	397.37	73.26	6.56	100.4	2.98	12.29	16.37
Patient No. 42 in add-on group patient	45	17.3	117	81	6	6.77	71.03	85.68	1755.32	26.6	82.8	0.71	13.65	14.2	3.79	561.22	342.2	93.33	7.56	128.3	3.74	9.83	14.55
Patient No. 43 in add-on group patient	60	28.26	123	75	5.3	5.8	84.8	73.32	1574.37	26.61	78	0.67	10.66	12.47	3.24	501.4	310.38	100.9	9.75	139.37	4.17	7.6	11.9

Supplementary Table 2. Original and individual data for **Table 2** in the manuscript

	FPG (mmol/L)	HbA_{1c} (%)	SBP (mmHg)	DBP (mmHg)
Patient No. 1 in conventional group	4.8	5.87	137	89
Patient No. 2 in conventional group	6	7.53	121	87
Patient No. 3 in conventional group	6.5	7.42	131	89
Patient No. 4 in conventional group	6	7.64	117	78
Patient No. 5 in conventional group	5.9	7.3	123	74
Patient No. 6 in conventional group	5.9	6.8	131	79
Patient No. 7 in conventional group	4.8	5.22	123	85
Patient No. 8 in conventional group	4.6	6.43	138	88
Patient No. 9 in conventional group	5.9	7.3	149	86
Patient No. 10 in conventional group	4.4	5.63	128	73
Patient No. 11 in conventional group	6.5	7.5	140	80
Patient No. 12 in conventional group	4.5	5.77	115	84
Patient No. 13 in conventional group	4.5	5.6	115	86
Patient No. 14 in conventional group	5.7	6.71	121	76
Patient No. 15 in conventional group	6	7.5	138	96
Patient No. 16 in conventional group	5.3	6.42	139	89
Patient No. 17 in conventional group	4.6	5.65	138	83
Patient No. 18 in conventional group	6.8	7	114	86
Patient No. 19 in conventional group	5.7	6.85	139	79
Patient No. 20 in conventional group	4.5	5.74	139	83
Patient No. 21 in conventional group	6	7.93	139	78
Patient No. 22 in conventional group	6.8	6.98	139	87
Patient No. 23 in conventional group	4.9	5.33	130	89
Patient No. 24 in conventional group	5.9	6.83	113	73
Patient No. 25 in conventional group	5.9	6.93	121	89
Patient No. 26 in conventional group	6.9	8.5	129	77
Patient No. 27 in conventional group	5	5.39	127	93
Patient No. 28 in conventional group	6.9	7.86	137	81
Patient No. 29 in conventional group	5.4	6.62	140	89
Patient No. 30 in conventional group	6.3	6.95	139	88
Patient No. 31 in conventional group	4.9	5.98	137	75
Patient No. 32 in conventional group	4.9	5.56	130	80
Patient No. 33 in conventional group	4.9	5.75	139	85
Patient No. 34 in conventional group	5.9	7.79	120	77
Patient No. 35 in conventional group	6.9	7.89	124	89
Patient No. 36 in conventional group	6	7.85	126	85
Patient No. 37 in conventional group	6	6.95	128	84
Patient No. 38 in conventional group	6	6.88	126	88
Patient No. 39 in conventional group	4.4	5.62	128	83
Patient No. 40 in conventional group	6	6.7	136	80
Patient No. 1 in add-on group patient	6.8	7.81	136	83
Patient No. 2 in add-on group patient	5.7	6.82	113	86
Patient No. 3 in add-on group patient	5.9	7	140	76
Patient No. 4 in add-on group patient	6.7	7.35	114	86
Patient No. 5 in add-on group patient	4.4	5.02	132	88
Patient No. 6 in add-on group patient	6.1	6.64	128	85
Patient No. 7 in add-on group patient	5.9	6.9	128	86
Patient No. 8 in add-on group patient	5.7	6.37	134	88
Patient No. 9 in add-on group patient	5.6	6.88	114	73
Patient No. 10 in add-on group patient	5.6	6.7	128	88
Patient No. 11 in add-on group patient	5.2	5.56	149	99
Patient No. 12 in add-on group patient	5.8	6.81	148	97

Patient No. 13 in add-on group patient	6.9	7.9	138	97
Patient No. 14 in add-on group patient	5.7	6.9	138	82
Patient No. 15 in add-on group patient	6	6.83	125	89
Patient No. 16 in add-on group patient	5.7	6.4	119	83
Patient No. 17 in add-on group patient	5.6	6.12	138	83
Patient No. 18 in add-on group patient	4.8	6.15	139	89
Patient No. 19 in add-on group patient	6.9	7	139	88
Patient No. 20 in add-on group patient	6	6.64	125	85
Patient No. 21 in add-on group patient	5.5	5.9	127	78
Patient No. 22 in add-on group patient	5.8	6.41	138	86
Patient No. 23 in add-on group patient	6	6.88	114	73
Patient No. 24 in add-on group patient	5.9	6.72	116	74
Patient No. 25 in add-on group patient	5.4	5.9	136	88
Patient No. 26 in add-on group patient	6	6.9	136	98
Patient No. 27 in add-on group patient	5.9	6.41	116	77
Patient No. 28 in add-on group patient	5.7	6.53	148	99
Patient No. 29 in add-on group patient	5.6	6.38	135	78
Patient No. 30 in add-on group patient	5.7	6.6	117	76
Patient No. 31 in add-on group patient	6.8	7.7	113	74
Patient No. 32 in add-on group patient	5.9	6.59	113	88
Patient No. 33 in add-on group patient	6	6.73	121	85
Patient No. 34 in add-on group patient	5.5	6.16	116	73
Patient No. 35 in add-on group patient	6	6.72	114	77
Patient No. 36 in add-on group patient	5.8	6.48	116	86
Patient No. 37 in add-on group patient	5.9	6.21	115	73
Patient No. 38 in add-on group patient	5	6.1	135	89
Patient No. 39 in add-on group patient	4.6	4.9	134	81
Patient No. 40 in add-on group patient	6	7.6	139	85
Patient No. 41 in add-on group patient	5.7	6.6	115	75
Patient No. 42 in add-on group patient	6	6.75	124	86
Patient No. 43 in add-on group patient	5.8	6.83	137	83

Supplementary Table 3. Original and individual data for **Table 3** in the manuscript

	eGFR (ml/min/1.73 m^2)	UACR (μg/mg)	KIM-1 (pg/mL)	NGAL (ng/mL)	Creatinine (μmol/L)	RI
Patient No. 1 in conventional group	-2.57	19.59	278.95	5.2	3.15	-0.01
Patient No. 2 in conventional group	-4.1	30.7	346.84	7.47	5.01	0.02
Patient No. 3 in conventional group	-4.62	32.85	356.9	7.88	5.34	0.02
Patient No. 4 in conventional group	-5.56	37.66	396.7	9.65	6.33	0.03
Patient No. 5 in conventional group	-4.01	31.48	331.8	7.33	5.46	0.02
Patient No. 6 in conventional group	-5.32	35.52	388.42	9.5	5.8	0.04
Patient No. 7 in conventional group	-3.35	26.74	312.58	6	3.51	0.02
Patient No. 8 in conventional group	-2.69	23.51	299.4	5.24	3.26	0.01
Patient No. 9 in conventional group	-3.89	30.09	368.3	7.66	5.13	0.02
Patient No. 10 in conventional group	-4.12	28.56	362.81	6.48	4.42	0.01
Patient No. 11 in conventional group	-8.03	41.82	433.59	9.82	7.14	0.04
Patient No. 12 in conventional group	-3.1	25.19	326.8	6.43	4.38	0.01
Patient No. 13 in conventional group	-2.13	23.11	318.93	5.58	4.01	0.02
Patient No. 14 in conventional group	-3.86	29	348.91	7.26	5.17	0.03
Patient No. 15 in conventional group	-7.63	42.03	457.67	9.52	8.02	0.04
Patient No. 16 in conventional group	-3.68	28.01	338.3	6.89	4.03	0.01
Patient No. 17 in conventional group	-2.45	20.15	285.5	5.04	3.84	0.01
Patient No. 18 in conventional group	-5.27	36	398.4	9.36	6.4	0.04
Patient No. 19 in conventional group	-4.66	34.82	386.54	8.01	5.8	0.03

Patient No. 20 in conventional group	-2.16	24.8	338.07	5.29	4.72	0.01
Patient No. 21 in conventional group	-4.98	34	395.17	8.28	5.98	0.03
Patient No. 22 in conventional group	-6.89	41.93	442.77	9.13	7.41	0.04
Patient No. 23 in conventional group	-3.34	27.53	321	6.44	4.62	0.02
Patient No. 24 in conventional group	-3.95	30	367.41	7.2	5.2	0.01
Patient No. 25 in conventional group	-2.25	22.19	285.93	5.3	4.26	0.01
Patient No. 26 in conventional group	-6.83	40.73	397.48	8.93	7.12	0.03
Patient No. 27 in conventional group	-2.36	20.33	290.34	5.48	3.4	0.01
Patient No. 28 in conventional group	-5.83	36.1	429.46	9.73	6.18	0.04
Patient No. 29 in conventional group	-2.55	20.4	301.5	5.46	3.48	0.02
Patient No. 30 in conventional group	-4.41	33.52	374.29	8.04	6.02	0.02
Patient No. 31 in conventional group	-4.04	32.54	347.92	7.93	5.73	0.02
Patient No. 32 in conventional group	-2.87	21.3	297.11	5.71	3.24	0.01
Patient No. 33 in conventional group	-3.49	26.3	316.26	6.6	4.62	0.02
Patient No. 34 in conventional group	-5.63	37.9	418.63	9.01	7.1	0.03
Patient No. 35 in conventional group	-6.77	41.32	439.89	10.03	8.03	0.04
Patient No. 36 in conventional group	-4.37	31.28	329.02	7.5	5.31	0.02
Patient No. 37 in conventional group	-5.01	34.66	396.41	7.83	6.4	0.02
Patient No. 38 in conventional group	-4.13	28.4	317.55	6.77	4.8	0.01
Patient No. 39 in conventional group	-3.85	25.53	280.3	6.9	3.69	0.02
Patient No. 40 in conventional group	-5.7	37.19	403.68	9.2	6.6	0.04
Patient No. 1 in add-on group patient	1.83	-10.55	-199.03	-3.76	-2.46	-0.05
Patient No. 2 in add-on group patient	2.39	-9.64	-192.76	-3.88	-2.38	0.02
Patient No. 3 in add-on group patient	2.01	-7.3	-188.27	-3.46	-2.17	-0.02
Patient No. 4 in add-on group patient	5.8	-14.31	-238	-6.15	-5.01	-0.05
Patient No. 5 in add-on group patient	4.87	-13.09	-233.97	-5.57	-4.13	-0.06
Patient No. 6 in add-on group patient	9.17	-16.34	-307.36	-8.13	-6.2	-0.06
Patient No. 7 in add-on group patient	2.35	-7.33	-180.9	-3.2	-2.55	-0.04
Patient No. 8 in add-on group patient	8.93	-15.29	-278.53	-6.34	-5.25	-0.07
Patient No. 9 in add-on group patient	2.26	-8.34	-201.69	-3.6	-2.48	-0.05
Patient No. 10 in add-on group patient	2.61	-9.77	-215.33	-4.3	-2.6	-0.04
Patient No. 11 in add-on group patient	4.73	-11	-208.58	-5.01	-4.15	-0.06
Patient No. 12 in add-on group patient	6.59	-15	-261.46	-7.01	-5.85	-0.05
Patient No. 13 in add-on group patient	7.01	-14.36	-259.32	-6.02	-5.83	-0.07
Patient No. 14 in add-on group patient	7.98	-16.27	-307.23	-7.25	-7.22	-0.07
Patient No. 15 in add-on group patient	8.41	-16.7	-301.6	-8.01	-6.59	-0.07
Patient No. 16 in add-on group patient	5.9	-14.06	-281.62	-6.03	-5	-0.05
Patient No. 17 in add-on group patient	4.8	-12.44	-241.79	-5.22	-4.04	-0.06
Patient No. 18 in add-on group patient	2.15	-8.76	-179.53	-4.08	-2.5	-0.05
Patient No. 19 in add-on group patient	6.89	-16.54	-299.69	-7.05	-5.57	-0.07
Patient No. 20 in add-on group patient	9.12	-19.42	-330.18	-8.2	-8.02	-0.07
Patient No. 21 in add-on group patient	5.13	-14.32	-276.19	-6.14	-5.1	-0.05
Patient No. 22 in add-on group patient	2.86	-10.46	-210.36	-5	-3.48	-0.03
Patient No. 23 in add-on group patient	5.02	-13.79	-268.1	-5.85	-4.22	-0.08
Patient No. 24 in add-on group patient	2.37	-9.89	-191.1	-4.39	-3.18	-0.05
Patient No. 25 in add-on group patient	5.03	-13	-250.34	-5.49	-3.97	-0.05
Patient No. 26 in add-on group patient	6.54	-16.34	-297.18	-7.19	-5.6	-0.07
Patient No. 27 in add-on group patient	3.02	-8.36	-193.36	-4.37	-2.05	-0.03
Patient No. 28 in add-on group patient	4.57	-12.2	-235.7	-4.01	-3.08	-0.06
Patient No. 29 in add-on group patient	5.41	-13	-241.92	-5.33	-3.88	-0.06
Patient No. 30 in add-on group patient	4.29	-11.1	-220	-5.07	-2.45	-0.05
Patient No. 31 in add-on group patient	4.67	-13.69	-249.3	-5.73	-4.06	-0.05
Patient No. 32 in add-on group patient	6.82	-15.35	-268.67	-6.43	-5.89	-0.06
Patient No. 33 in add-on group patient	7.39	-16.59	-282.3	-7.31	-5.79	-0.06
Patient No. 34 in add-on group patient	6.01	-15.2	-278	-6.7	-6.33	-0.08

Patient No. 35 in add-on group patient	7.05	-15.82	-261	-6.9	-5.94	-0.06
Patient No. 36 in add-on group patient	7.64	-16.48	-291.02	-7.53	-5.88	-0.07
Patient No. 37 in add-on group patient	7.43	-17.42	-315.01	-8.06	-6.59	-0.06
Patient No. 38 in add-on group patient	5.01	-13.3	-231.89	-5.63	-3.22	-0.05
Patient No. 39 in add-on group patient	3.89	-12	-211.36	-5.3	-4.05	-0.06
Patient No. 40 in add-on group patient	4.99	-14.32	-255.2	-6.06	-4.61	-0.08
Patient No. 41 in add-on group patient	5.72	-16.3	-298.35	-7.94	-6.34	-0.05
Patient No. 42 in add-on group patient	6.03	-15.2	-249.57	-7.33	-5.7	-0.06
Patient No. 43 in add-on group patient	3.62	-10.33	-198.04	-4.36	-2.17	-0.04

Supplementary Table 4. Original and individual data for **Table 4** in the manuscript

	TNF-α (pg/mL)	IL-6 (pg/mL)	H-CRP (μg/mL)	VCAM-1 (ng/mL)	MCP-1 (pg/mL)
Patient No. 1 in conventional group	2.2	1.8	0.29	70	36.31
Patient No. 2 in conventional group	3.14	2.45	0.51	76.35	46.88
Patient No. 3 in conventional group	3.79	2.66	0.48	84.52	50.51
Patient No. 4 in conventional group	4.41	3.22	0.61	87.2	52.6
Patient No. 5 in conventional group	3.93	2.57	0.5	78.42	40.26
Patient No. 6 in conventional group	4.02	3.09	0.63	84.29	49.1
Patient No. 7 in conventional group	2.77	2.48	0.38	76.3	39.61
Patient No. 8 in conventional group	2.19	1.96	0.35	61.73	30.5
Patient No. 9 in conventional group	3.8	2.55	0.55	84.94	46.38
Patient No. 10 in conventional group	2.35	2.16	0.46	81.62	43.62
Patient No. 11 in conventional group	5.02	2.69	0.83	101.3	70.04
Patient No. 12 in conventional group	2.3	2	0.43	63.28	32.2
Patient No. 13 in conventional group	2.74	2.4	0.36	68.93	34.41
Patient No. 14 in conventional group	3.41	2.69	0.49	78.35	36.49
Patient No. 15 in conventional group	5.13	4.13	0.97	99.47	60.09
Patient No. 16 in conventional group	3.12	2.33	0.45	75.68	37.1
Patient No. 17 in conventional group	2.68	1.99	0.36	62.16	30.25
Patient No. 18 in conventional group	4.33	2.93	0.63	92.55	50.29
Patient No. 19 in conventional group	3.2	2.58	0.59	86.49	46.41
Patient No. 20 in conventional group	2.67	2.29	0.39	69.58	38.56
Patient No. 21 in conventional group	3.41	3.14	0.6	88.35	48.94
Patient No. 22 in conventional group	5.14	3.86	0.91	106.37	58.37
Patient No. 23 in conventional group	2.98	2.27	0.54	74.81	35.34
Patient No. 24 in conventional group	3.49	2.62	0.52	76.98	40.18
Patient No. 25 in conventional group	2.79	1.89	0.3	65.8	37.44
Patient No. 26 in conventional group	3.87	3.6	0.86	97.53	51.27
Patient No. 27 in conventional group	3.01	2.01	0.35	66.27	33.96
Patient No. 28 in conventional group	5.55	3.05	0.7	96.38	51.9
Patient No. 29 in conventional group	3.49	2.29	0.38	63.1	30
Patient No. 30 in conventional group	4.1	2.59	0.58	88.94	40.26
Patient No. 31 in conventional group	3.75	3.03	0.61	86.02	46.52
Patient No. 32 in conventional group	2.58	2.7	0.33	59.38	35.9
Patient No. 33 in conventional group	2.9	2.89	0.47	61.68	29.01
Patient No. 34 in conventional group	4.14	3.64	0.63	98.34	47.02
Patient No. 35 in conventional group	6.03	3.93	0.64	97.25	50.1
Patient No. 36 in conventional group	4.32	2.61	0.59	80.77	45.33
Patient No. 37 in conventional group	3.88	3.29	0.55	88.26	42.77
Patient No. 38 in conventional group	3.46	2.33	0.4	75.04	43.14
Patient No. 39 in conventional group	2.2	2.51	0.38	60.86	31.8
Patient No. 40 in conventional group	4.53	2.88	0.75	90.33	52.15
Patient No. 1 in add-on group patient	-1.77	-1.39	-0.36	-70.3	-27.51

Patient No. 2 in add-on group patient	-1.64	-1.7	-0.31	-50.34	-21.09
Patient No. 3 in add-on group patient	-1.56	-1.55	-0.29	-71.43	-19.6
Patient No. 4 in add-on group patient	-2.9	-2.19	-0.43	-121.48	-33.2
Patient No. 5 in add-on group patient	-2.05	-2	-0.45	-101.38	-27.54
Patient No. 6 in add-on group patient	-3.5	-3.15	-0.58	-122.03	-39.31
Patient No. 7 in add-on group patient	-2	-1.6	-0.3	-60.63	-21.71
Patient No. 8 in add-on group patient	-3.01	-2.63	-0.45	-140.52	-33.26
Patient No. 9 in add-on group patient	-2.1	-1.88	-0.31	-69.55	-19.92
Patient No. 10 in add-on group patient	-1.78	-1.23	-0.35	-89.62	-29.33
Patient No. 11 in add-on group patient	-2.34	-1.89	-0.38	-88.39	-24.9
Patient No. 12 in add-on group patient	-3.62	-2.35	-0.49	-138.32	-35.17
Patient No. 13 in add-on group patient	-3.07	-2.26	-0.44	-128.36	-33.14
Patient No. 14 in add-on group patient	-4.02	-2.8	-0.51	-139.91	-40.25
Patient No. 15 in add-on group patient	-3.7	-2.64	-0.6	-135.38	-36.79
Patient No. 16 in add-on group patient	-2.6	-2.11	-0.43	-121.52	-30.61
Patient No. 17 in add-on group patient	-2.3	-1.77	-0.39	-86.3	-26.89
Patient No. 18 in add-on group patient	-1.58	-1.2	-0.3	-78.66	-22.51
Patient No. 19 in add-on group patient	-3.36	-2.89	-0.55	-138.23	-40.38
Patient No. 20 in add-on group patient	-4.7	-3.02	-0.6	-161.37	-44.55
Patient No. 21 in add-on group patient	-3.73	-2.03	-0.46	-130.36	-37.81
Patient No. 22 in add-on group patient	-2.5	-1.44	-0.3	-70.92	-26.82
Patient No. 23 in add-on group patient	-2.47	-1.86	-0.4	-115.82	-31.62
Patient No. 24 in add-on group patient	-2.3	-1.28	-0.32	-60.41	-25.18
Patient No. 25 in add-on group patient	-2.57	-1.73	-0.46	-117.99	-28.29
Patient No. 26 in add-on group patient	-3.63	-2.48	-0.54	-138.43	-32.13
Patient No. 27 in add-on group patient	-1.93	-1.36	-0.31	-51.33	-30.31
Patient No. 28 in add-on group patient	-2.02	-1.45	-0.39	-89.35	-21.38
Patient No. 29 in add-on group patient	-2.46	-1.37	-0.41	-118.3	-35.54
Patient No. 30 in add-on group patient	-2.2	-1.64	-0.42	-95.33	-30.97
Patient No. 31 in add-on group patient	-2.01	-1.78	-0.4	-105.33	-35.11
Patient No. 32 in add-on group patient	-3.29	-2.49	-0.53	-138.27	-34
Patient No. 33 in add-on group patient	-3.37	-3.02	-0.5	-154.09	-38.14
Patient No. 34 in add-on group patient	-3	-2.75	-0.48	-118.41	-33
Patient No. 35 in add-on group patient	-3.19	-2.56	-0.48	-129.5	-34.61
Patient No. 36 in add-on group patient	-3.5	-3.04	-0.5	-132.9	-39.1
Patient No. 37 in add-on group patient	-5.01	-3.5	-0.65	-154.96	-39.65
Patient No. 38 in add-on group patient	-2.19	-1.89	-0.46	-106.4	-25.76
Patient No. 39 in add-on group patient	-1.98	-1.47	-0.35	-110	-25
Patient No. 40 in add-on group patient	-2.25	-2.13	-0.4	-117.37	-30.14
Patient No. 41 in add-on group patient	-3.64	-2.29	-0.49	-131.28	-34.97
Patient No. 42 in add-on group patient	-3.22	-2.7	-0.49	-135.39	-37.07
Patient No. 43 in add-on group patient	-2.5	-1.5	-0.31	-64.2	-21.66

Supplementary Table 5. Original and individual data for **Table 5** in the manuscript

	HO-1 (μmol/L)	Bilirubin (μmol/L)	GSH-Px (U/L)	T-AOC (U/mL)	U-8-OHdG	MDA (nmmol/mL)
Patient No. 1 in conventional group	-2.98	-1.77	-4.06	-0.21	0.83	0.61
Patient No. 2 in conventional group	-4.9	-1.56	-5.02	-0.28	0.95	0.8
Patient No. 3 in conventional group	-5.52	-1.3	-5.13	-0.31	1.1	0.88
Patient No. 4 in conventional group	-6.33	-0.92	-6.28	-0.38	1.3	1.01
Patient No. 5 in conventional group	-4.79	-1.44	-5.1	-0.29	0.93	0.84
Patient No. 6 in conventional group	-5.86	-1.1	-5.86	-0.34	0.99	0.93
Patient No. 7 in conventional group	-4.38	-1.27	-3.69	-0.24	0.82	0.53

Patient No. 8 in conventional group	-3.82	-1.2	-3.41	-0.26	0.78	0.65
Patient No. 9 in conventional group	-4.89	-1.32	-4.86	-0.25	1.03	0.81
Patient No. 10 in conventional group	-4.36	-1.2	-5.25	-0.23	0.89	0.85
Patient No. 11 in conventional group	-7.93	-1.82	-5.83	-0.4	1.46	1.4
Patient No. 12 in conventional group	-4.49	-1.72	-4.63	-0.21	0.88	0.65
Patient No. 13 in conventional group	-3.92	-1.52	-4.25	-0.22	0.8	0.6
Patient No. 14 in conventional group	-4.68	-1.23	-4.32	-0.27	0.95	0.68
Patient No. 15 in conventional group	-7.42	-1.85	-8.02	-0.45	1.45	1.23
Patient No. 16 in conventional group	-5.31	-1.14	-4.43	-0.34	0.91	0.74
Patient No. 17 in conventional group	-2.85	-1.68	-4.52	-0.26	0.83	0.66
Patient No. 18 in conventional group	-7.66	-1.19	-5.89	-0.39	1.28	1.09
Patient No. 19 in conventional group	-5.9	-1.44	-5.53	-0.32	1.06	1.12
Patient No. 20 in conventional group	-4.43	-1.17	-4	-0.27	0.8	0.7
Patient No. 21 in conventional group	-5.82	-1.63	-5.59	-0.36	1.13	0.98
Patient No. 22 in conventional group	-7.57	-0.99	-7.22	-0.44	1.45	1.13
Patient No. 23 in conventional group	-4.31	-1.2	-3.68	-0.23	0.79	0.83
Patient No. 24 in conventional group	-5.52	-1.3	-5.36	-0.34	1.01	0.86
Patient No. 25 in conventional group	-4.2	-1.63	-3.51	-0.28	0.92	0.55
Patient No. 26 in conventional group	-7.64	-1.25	-7.35	-0.36	1.36	1.05
Patient No. 27 in conventional group	-3.67	-1.83	-3.02	-0.23	0.78	0.62
Patient No. 28 in conventional group	-5.93	-1.7	-6.33	-0.33	1.29	0.97
Patient No. 29 in conventional group	-3.66	-1.01	-4.04	-0.25	0.9	0.75
Patient No. 30 in conventional group	-5.38	-1.5	-5.19	-0.36	1.11	0.85
Patient No. 31 in conventional group	-5.21	-1.66	-5.46	-0.31	1.24	0.9
Patient No. 32 in conventional group	-3.62	-1.6	-3.67	-0.27	0.96	0.77
Patient No. 33 in conventional group	-4.15	-1.13	-4.69	-0.22	0.85	0.84
Patient No. 34 in conventional group	-6.92	-1.08	-7.07	-0.35	1.33	1.09
Patient No. 35 in conventional group	-7.69	-1.03	-8.05	-0.39	1.36	1.05
Patient No. 36 in conventional group	-5.41	-1.32	-5.01	-0.24	0.93	0.83
Patient No. 37 in conventional group	-6.72	-1.57	-5.85	-0.26	1.14	0.92
Patient No. 38 in conventional group	-4.63	-1.62	-5.23	-0.29	1.16	0.79
Patient No. 39 in conventional group	-3.52	-1.26	-4.58	-0.28	0.84	0.9
Patient No. 40 in conventional group	-6.4	-1.19	-7.1	-0.35	1.39	0.94
Patient No. 1 in add-on group patient	5.26	1.39	12.79	0.45	-1.51	-1.56
Patient No. 2 in add-on group patient	5.55	1.5	13.02	0.32	-1.43	-1.6
Patient No. 3 in add-on group patient	5.66	1.28	12.57	0.36	-1.39	-1.49
Patient No. 4 in add-on group patient	8.31	2.3	22.15	0.58	-1.89	-1.88
Patient No. 5 in add-on group patient	7.88	1.98	16.62	0.49	-2.01	-2.01
Patient No. 6 in add-on group patient	8.57	3.03	23.78	0.68	-2.4	-2.36
Patient No. 7 in add-on group patient	5.53	1.67	14.03	0.34	-1.37	-1.51
Patient No. 8 in add-on group patient	9.54	2.31	21.47	0.65	-2.11	-2.01
Patient No. 9 in add-on group patient	5.3	1.47	13.6	0.41	-1.41	-1.72
Patient No. 10 in add-on group patient	5.92	2.1	12.51	0.38	-1.55	-1.6
Patient No. 11 in add-on group patient	6.58	1.93	15.83	0.49	-1.39	-1.59
Patient No. 12 in add-on group patient	10.01	2.56	21.49	0.55	-2.25	-1.99
Patient No. 13 in add-on group patient	8.13	2.21	19.3	0.53	-1.9	-2.03
Patient No. 14 in add-on group patient	8.92	3.31	25.58	0.61	-2.38	-2.25
Patient No. 15 in add-on group patient	9.05	2.84	23.56	0.7	-2.46	-2.59
Patient No. 16 in add-on group patient	8	2.1	17.93	0.58	-2.08	-2.57
Patient No. 17 in add-on group patient	7.13	1.91	15.59	0.48	-1.37	-1.69
Patient No. 18 in add-on group patient	5.93	1.48	13.66	0.41	-1.37	-1.6
Patient No. 19 in add-on group patient	8.62	2.68	23.81	0.64	-2.8	-2.25
Patient No. 20 in add-on group patient	10.3	3.14	25.68	0.78	-3.4	-2.42
Patient No. 21 in add-on group patient	7.69	2.3	18.27	0.47	-2.14	-2
Patient No. 22 in add-on group patient	5.77	1.57	14.49	0.36	-1.29	-1.65

Patient No. 23 in add-on group patient	8.02	2.2	18.21	0.46	-1.65	-1.93
Patient No. 24 in add-on group patient	6.6	1.79	15	0.35	-1.43	-1.57
Patient No. 25 in add-on group patient	7.93	1.98	20.4	0.52	-2.05	-1.81
Patient No. 26 in add-on group patient	8.46	2.95	23.59	0.6	-2.5	-2.39
Patient No. 27 in add-on group patient	5.37	1.62	13.01	0.39	-1.4	-1.6
Patient No. 28 in add-on group patient	6.52	2.01	14.92	0.39	-1.52	-1.71
Patient No. 29 in add-on group patient	7.84	2.41	19.26	0.47	-1.88	-1.95
Patient No. 30 in add-on group patient	6.79	1.66	12.33	0.42	-1.59	-1.63
Patient No. 31 in add-on group patient	7.42	2.1	20	0.49	-1.76	-1.88
Patient No. 32 in add-on group patient	8.25	2.55	22.63	0.6	-2.54	-2.06
Patient No. 33 in add-on group patient	9.63	2.6	23.53	0.7	-2.71	-2.61
Patient No. 34 in add-on group patient	8.32	2.31	20.68	0.64	-2.07	-2.27
Patient No. 35 in add-on group patient	7.9	2.52	19.43	0.59	-2.42	-2.19
Patient No. 36 in add-on group patient	8.92	2.66	21.73	0.59	-2.08	-2.34
Patient No. 37 in add-on group patient	9.48	2.83	21.57	0.63	-2.84	-2.5
Patient No. 38 in add-on group patient	7.26	2.19	16.36	0.49	-1.83	-1.83
Patient No. 39 in add-on group patient	7.4	1.77	15.6	0.42	-1.44	-1.6
Patient No. 40 in add-on group patient	7.54	1.52	17.26	0.51	-2.03	-1.73
Patient No. 41 in add-on group patient	8.61	2.43	20.61	0.57	-2.13	-2.12
Patient No. 42 in add-on group patient	8.91	2.56	19.35	0.53	-2	-2.09
Patient No. 43 in add-on group patient	6.27	1.73	13.7	0.38	-1.33	-1.4