Table I. Clinical response to IV tPA.

	Good response			Dramatic response		
	Yes (n=76)	No (n=69)	*P*	Yes (n=41)	No (n=104)	*P*
Age	69 ± 13	70 ± 13	*0,672*	70 ± 15	69 ± 13	*0,920*
Gender, female	55%	55%	*0,982*	61%	53%	*0,378*
VKİ	27,9 ± 6,1	27,5 ± 5,1	*0,742*	28,6 ± 7,1	27,3 ± 4,8	*0,281*
Hypertension	65%	73%	*0,302*	56%	73%	*0,048*
Diabetes	20%	29%	*0,228*	20%	27%	*0,352*
Atrial fibrillation	29%	38%	*0,264*	29%	35%	*0,538*
Cardioembolism	58%	59%	*0.924*	55%	60%	*0,632*
Symptom-to-door duration (min)	77 ± 40	82 ± 46	*0,691*	91 ± 49	76 ± 39	*0,058*
NIHSS arrival	13,6 ± 5,5	14,7 ± 5, 9	*0,239*	13,2 ± 5,9	14,5 ± 5,6	*0,219*
Symptom-to-needle duration (min)	150 ± 54	171 ± 61	*0,030*	164 ± 67	159 ± 54	*0,626*
Hospitalization duration	16 ± 25	27 ± 28	*0,016*	12 ± 19	25 ± 28	*0,004*
Any hemorrhage	18%	37%	*0,010*	10%	35%	*0,003*
PH2	1%	13%	*0,005*	0%	10%	*0,040*
M1 / TICA / BA occlusion	43%	55%	*0,161*	42%	52%	*0.257*
No occlusion	21%	12%	*0.126*	29%	12%	*0,010*
Parameters of glycemia						
HbA1c	6,14 ± 1,05	6,48 ± 1,32	*0,215*	5,91 ± 0,91	6,45 ± 1,25	*0,057*
Pre-treatment BG	140 ± 57	147 ± 54	*0,497*	139 ± 47	145 ± 58	*0,600*
24-hour average BG	132 ± 45	138 ± 44	*0,451*	125 ± 36	139 ± 47	*0,067*
24-hour BG SD	20,52 ± 26,28	21,97 ± 24,84	*0,742*	20,71 ± 29,98	21,41 ± 23,73	*0,887*
24-hour BG CV	0,18 ± 0,16	0,18 ± 0,14	*0,892*	0,2 ± 0,18	0,17 ± 0,14	*0,326*
J-index	29,25 ± 26,4	28,39 ± 18,28	*0,843*	30,14 ± 25,32	28,43 ± 22,02	*0,735*

Abbreviations; BA: Basilar artery; CV: Coefficient of Variation; Min: Minute; HbA1c:Hemoglobin A1c; ICA:internal carotid artery; IV: Intravenous; BG: Blood Glucose; M1: middle cerebral artery (MCA) first segment; NIHSS: National Institute of Health Stroke Scale; PH2:Parenchymal hematoma type-2; SD:Standard deviation; tPA: tissue plasminogen activator; BMI: Body Mass Index.

Table II. Clinical outcomes with IV tPA.

	Perfect outcome [mRS≤1]			Good outcome [mRS≤2]		
	Yes (n=48)	No (n=96)	*P*	Yes (n=67)	No (n=78)	*P*
Age	65 ± 14	72 ± 12	*0,004*	66 ± 14	72 ± 12	*0,004*
Gender, female	58%	53%	*0,554*	52%	52%	*0,555*
BMI	27,4 ± 5,1	27,9 ± 5,9	*0,658*	29,0 ± 6,9	26,7 ± 4,2	*0,050*
Hypertension	50%	77%	*0.001*	58%	77%	*0,018*
Diabetes	21%	27%	*0,414*	24%	36%	*0.772*
Atrial fibrillation	31%	34%	*0,708*	27%	39%	*0.125*
Cardioembolism	55%	61%	*0.488*	55%	63%	*0.394*
Symptom-to-door duration (min)	83 ± 44	79 ± 43	*0,568*	84 ± 48	77 ± 38	*0,334*
NIHSS arrival	11,8 ± 5,7	15,3 ± 5,4	*<0,001*	11,6 ± 5,3	16,4 ± 5,1	*<0,001*
Symptom-to-needle duration (min)	158 ± 62	162 ± 57	*0,670*	160 ± 62	161 ± 55	*0,845*
Hospitalization duration	10 ± 6	26 ± 31	*0,001*	11 ± 6	30 ± 33	*<0,001*
Any hemorrhage	15%	34%	*0,112*	18%	36%	*0,016*
PH2	0%	10%	*0,020*	0%	13%	*0,002*
M1 / TICA / BA occlusion	40%	53%	*0.125*	39%	57%	*0.028*
No occlusion	23%	14%	*0,155*	20%	14%	*0,411*
Parameters of glycemia						
HbA1c	6 ± 0,84	6,44 ± 1,32	*0,119*	6,13 ± 0,92	6,44 ± 1,4	*0,268*
Pre-treatment BG	132 ± 44	148 ± 60	*0,153*	135 ± 45	151 ± 63	*0,131*
24-hour average BG	121 ± 34	142 ± 48	*0,008*	124 ± 34	145 ± 51	*0,005*
24-hour BG SD	20,8 ± 29,42	21,59 ± 23,65	*0,573*	20,84 ± 26,49	21,79 ± 24,91	*0,830*
24-hour BG CV	0,19 ± 0,18	0,17 ± 0,14	*0,509*	0,18 ± 0,16	0,18 ± 0,15	*0,817*
J-index	26,25 ± 23,4	30,25 ± 22,56	*0,393*	25,82 ± 21,12	31,99 ± 24,09	*0,155*

Abbreviations; BA: Basilar artery; CV: Coefficient of Variation; Min:Minute; HbA1c: Hemoglobin A1c; ICA: internal carotid artery; IV: Intravenous; BG: Blood Glucose; M1: middle cerebral artery (MCA) first segment; NIHSS: "National Institute of Health Stroke Scale"; PH2: Parenchymal hematoma type-2; SD: Standard deviation; tPA: tissue plasminogen activator; BMI: Body Mass Index.

Table III. Post IV tPA hemorrhage.

	Hemorrhage			PH type 2		
	Yes (n=40)	No (n=105)	*P*	Yes (n=10)	No (n=135)	*P*
Age	69 ± 12	70 ± 14	*0,950*	69 ± 14	70 ± 13	*0,845*
Gender, female	63%	53%	*0,294*	50%	56%	*0,718*
BMI	27,1 ± 4,6	27,9 ± 5,9	*0,580*	25,5 ± 4,1	27,9 ± 5,7	*0,284*
Hypertension	73%	67%	*0,522*	60%	69%	*0,549*
Diabetes	28%	24%	*0,624*	20%	25%	*0,723*
Atrial fibrillation	48%	27%	*0,021*	30%	33%	*0,841*
Cardioembolism	63%	56%	*0,477*	50%	59%	*0,614*
Symptom-to-door duration (min)	70 ± 37	85 ± 45	*0,056*	64 ± 39	82 ± 44	*0,194*
NIHSS arrival	15,6 ± 4,7	13,5 ± 6	*0,046*	16,6 ± 4,2	13,4 ± 5,8	*0,143*
Symptom-to-needle duration (min)	157 ± 49	161 ± 61	*0,743*	152 ± 46	161 ± 59	*0,631*
Hospitalization duration	24 ± 26	20 ± 27	*0,367*	35 ± 48	20 ± 24	*0,092*
M1 / TICA / BA occlusion	58%	45%	*0,188*	60%	48%	*0,456*
No occlusion	8%	20%	*0,073*	10%	17%	*0,569*
Parameters of glycemia						
HbA1c	6,48 ± 0,85	6,22 ± 1,24	*0,433*	6,33 ± 0,74	6,27 ± 1,19	*0,923*
Pre-treatment BG	135 ± 35	146 ± 60	*0,347*	153 ± 38	143 ± 56	*0,651*
24-hour average BG	140 ± 31	133 ± 49	*0,342*	161 ± 37	133 ± 45	*0,045*
24-hour BG SD	19,51 ± 23,76	21,9 ± 26,11	*0,628*	24 ± 25,03	21,04 ± 25,54	*0,726*
24-hour BG CV	0,16 ± 0,14	0,18 ± 0,16	*0,578*	0,2 ± 0,16	0,18 ± 0,15	*0,741*
J-index	28,98 ± 17,14	28,72 ± 24,44	*0,958*	38,08 ± 14,54	28,08 ± 23,05	*0,230*

Abbreviations; BA: Basilar artery; CV: Coefficient of Variation; Min: Minute; HbA1c: Hemoglobin A1c; ICA: internal carotid artery; IV: Intravenous; BG: Blood Glucose; M1: middle cerebral artery (MCA) first segment; NIHSS: "National Institute of Health Stroke Scale";PH2: Parenchymal hematoma type-2; SD: Standard deviation; tPA: tissue plasminogen activator; BMI: Body Mass Index.

mg/dL band within the first 24 hours in the guidelines for acute ischemic treatment [32].This is considered as a quality metric.

High blood glucose level is a common incident in the hyperacute period following an ischemic stroke and is considered to be an indicator of acute stress response. Hyperglycemic patients also benefit from IV tPA; however, high level of glucose reduces the effectiveness of thrombolytic therapy [4, 29-31]. In case of high blood glucose, the re-canalization creating and/or enhancing effect of tPA decreases, and a resistance is developed against thrombolytic agent. The first coming the mind out of the factors playing a role here is the the fact that the level of plasminogen activator inhibitor-type 1 (PAI-1) increases due to high blood glucose and hyperinsulism in diabetes and antagonizes tPA. In other words, fibrinolysis decreases in hyperglycemia [33]. Besides, the hyperglycemia directly increasing the coagulation and decreasing penumbral vasodilatation reduces the success of reperfusion. [23] When recanalization and reperfusion are ensured, high blood glucose level and/or its remaining at high levels increases the reperfusion damage and facilitates the development of hemorrhagic complications. Hyperglycemia-induced or increased oxidative stress, lactate accumulation, and tissue acidosis, increased matrix metalloproteinase level may be mediating this effect [23, 34]. On the basis of all these physiopathological logical explanations, we can mention that large scaled studies are required on determination of post-stroke blood glucose target values in hyperacute period, specific to the patients who were administered with IV tPA.

It was observed in our study that the basic glycemic variability parameters and their response to IV tPA are not related. This is not a subject studied in detail in the literature [14, 23]. It was addressed in a study, similar to our finding, that the average blood glucose level is important for the response to IV tPA, however BGSD is not a significant determinant as a GV indicator [35]. In another study, it was reported that J-index values are important in increasing cardiovascular mortality in these patients [20]. Glycemic variability is known to have an effect in a way to increase the vascular complications of diabetes in long term over various mechanisms, particularly oxidative stress [14, 17, 23, 28, 36]. Poor micro- and macrovascular status has the potential to adversely affect the prognosis of acute stroke. On the other hand, in at least three retrospective studies, the positive association between GV and increased mortality in ICU patients were shown to be more prominent in non-diabetic patients [15, 37-39]. In addition, a similar association was also observed in cases with traumatic brain injury [40]. Therefore, the same situation could be expected in

acute stroke cases who were administered with IV tPA, however, this was not supported by initial data. Preferably prospective and large-scale studies in more diverse designs should be planned to elucidate this problem.

Considering the evaluation of our results, it is necessary to address some limitations of our study. First of all, this is a retrospective analysis; a single-center data and the number of patients is "median" for such studies. In addition, the recanalization could not be documented for each patient. Moreover, as "post-stroke" hyperglycemia shows a positive correlation with acute stress response and more importantly with the cerebral infarction size, it was claimed that there is a epiphenomen in terms of prognosis [41]. However, we did not receive neuroimagings for consideration. Most importantly, the number of blood glucose measurements in our study was low and limited to 2-4 measurements in most of the patients. By the increase of this number and periodical checks in certain intervals, basic GV parameters, particularly BG standard deviation, could be more important. Lastly, the nutrition, fluid infusion and insulin administration for the patients were not recorded. Despite all these limitations, our study showed that the high level of blood glucose, rather than variability thereof, has a role on the efficacy of IV tPA. It would be efficient to test this data on a large scale.

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