Medical Certification of Pilots Through the Insulin-Treated Diabetes Mellitus Protocol at the FAA

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INTRODUCTION: In 2019, the Federal Aviation Administration (FAA) announced a protocol to evaluate pilots with insulin treated diabetes mellitus (ITDM) for special issuance (SI) medical certification for first-/second-class pilots. The protocol's aim is improved assessment of ITDM control/hypoglycemia risk and relies on continuous glucose monitoring (CGM) data. This study compares the characteristics of first-/second-class pilots with ITDM and certification outcome.

METHODS: Data was collected retrospectively from the FAA Document Imaging Workflow System (DIWS) for pilots considered for a first-/second-class SI under the ITDM program between November 2019 and October 2021. Inclusion criteria required submission of information required for certification decision (SI vs. denial). We extracted data on demographics and CGM parameters including mean glucose, standard deviation, coefficient of variance, time in range (%), time > 250 mg · dl^{-1} (%), and time < 70–80 mg · dl^{-1} (%). We compared these parameters between pilots issued an SI vs. denial with Mann-Whitney U-tests and Fisher exact tests using R.

RESULTS: Of 200 pilots with ITDM identified, 77 met inclusion criteria. Of those, 55 received SIs and 22 were denied. Pilots issued SI were statistically significantly older (46 vs. 27 yr), had a lower hemoglobin A1c (6.50% vs. 7.10%), lower average glucose (139 mg · dl^{-1} vs. 156 mg · dl^{-1}), and spent less time with low glucose levels (0.95% vs. 2.0%).

DISCUSSION: The FAA program has successfully medically certificated pilots with ITDM for first-/second-class. Pilots granted an ITDM SI reflect significantly better diabetes control, including less potential for hypoglycemia. As this program continues, it will potentially allow previously disqualified pilots to fly safely.

KEYWORDS: insulin-treated diabetes, continuous glucose monitoring, first class pilot medical certification, second class pilot medical certification.

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Insulin treated diabetes mellitus (ITDM) is a challenge to the Federal Aviation Administration (FAA) and other civil aviation authorities worldwide charged with medically evaluating pilots for performance of safety sensitive flight duties. ITDM is particularly challenging due to variability in pathogenesis, clinical presentation, treatment, side effects, and short- and long-term complications. Of particular concern is the potential for hypoglycemia which may go unrecognized and result in sudden and subtle incapacitation. The aerospace environment also poses challenges to pilots with diabetes. For example, sudden aircraft cabin depressurization may potentially cause insulin pumps to malfunction and release an insulin bolus.[10] Altitude and hypobaric hypoxia cause changes in blood glucose levels.[21] The aerospace environment has also been shown to worsen diabetic cystoid macular edema[6] and spaceflight has been associated with insulin resistance.[23]

For any medical condition, the FAA's main certification goal is to prevent sudden or subtle incapacitation of the pilot in flight that jeopardizes flight safety and endangers the lives of not only the pilots and passengers, but also those on the ground should an aircraft crash. Diabetes presents several mechanisms potentially concerning for incapacitation, including hypoglycemia, hyperglycemia, and macrovascular and microvascular

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complications. Specifically, hypoglycemia is the complication of greatest concern since it may cause impaired decision-making, disorientation, poor performance at cognitive skills, confusion, and loss of consciousness. Additionally, hypoglycemic unawareness has been observed in up to 40% of patients with type 1 diabetes and this unawareness increases the risk of severe hypoglycemia sixfold for these patients.[15] Consequences of severe hypoglycemia may include seizure, coma, cardiac dysrhythmias, and death.[15]

The goal of medical providers outside of aviation is to maintain effective glycemic control to mitigate irreversible diabetic complications, but tighter glycemic control increases the risk of hypoglycemic events.[20] Alternatively, hyperglycemia may cause short term adverse effects, including vision and refractive changes, poor cognition, and diabetic ketoacidosis, as well as long term hazards to aviation safety secondary to end organ complications.[9] Macrovascular and microvascular changes often occur in the heart, eye, kidneys, and peripheral nerves. Of particular concern in pilots is diabetic retinopathy, which, if unrecognized, may result in loss of vision critical to pilot duties. Diabetic neuropathy may subtly affect a pilot's ability to manipulate the controls. While chronic kidney disease is quite unlikely to result in an unforeseen incapacitating event, diabetes is significantly associated with myocardial infarction and other vascular events (e.g., stroke). ITDM also presents logistical challenges for pilots, including maintaining a diet while traveling, in-flight glucose monitoring, and postcrash survival considerations.

Other civil aviation authorities have attempted to address aeromedical concerns of ITDM. Canada was the first country to establish an ITDM protocol for first class pilots in 2002, followed by the United Kingdom in 2012.[21] These two countries relied on multicrew restrictions and/or notification of their copilot of their diabetes. A policy of ITDM for commercial pilots in the United States has been significantly more challenging.

In the United States, ITDM is a "specifically disqualifying" condition under Title 14 of the Code of Federal Regulations part 67 (14 CFR 67). However, pilots with specifically disqualifying conditions may be considered for authorization of a special issuance (SI) medical certificate. Prior to 1996, the FAA did not grant SI certifications to pilots with ITDM mainly due to concern for risk of hypoglycemia. In 1996, the FAA began granting special issuance medical certification for third-class (general aviation) duties for pilots with ITDM using a protocol for monitoring serum blood sugar levels.[21] This protocol requires finger stick blood glucose testing 30 min before takeoff, during flight, and before landing. The protocol recommended pilots maintain glucose levels above 120 mg $\cdot$ dL^{-1} during flight to avoid hypoglycemic events in the air. Notably, this recommended blood glucose target during flight is higher than the recommended routine medical management as a mitigation to minimize the risk for hypoglycemia.

Though the FAA experience with third-class medical certification has not proven overtly unsafe, developing a policy for ITDM for first- or second-class commercial pilot duties was challenging. Concerns included: 14 CFR 67 mandates that less risk is acceptable for commercial pilot duties; hypoglycemia risk increases with tight glucose control; inability to assess glycemic variability; and hypoglycemia unawareness and associated autonomic failure. In addition, U.S. case law in 1980 (Delta Airline v. United States) prohibited the FAA from setting operational limitations on first-class medical certificates. However, after several years of consideration, in November 2019 the FAA announced a new protocol to evaluate pilots with ITDM for SI medical certification for first-/second-class pilot duties. The protocol's aim was to introduce an improved method for assessment of ITDM control (especially glycemic variability) and the attendant risks for hypoglycemia. The criteria for the protocol include clinical stability for at least 6 mo on the current treatment regimen and relies in part on pilot continuous glucose monitoring (CGM) data, both in the air and while on the ground. The goal of requiring CGM was in part to align diabetes management both in and out of the flight deck as well as to use longitudinal data demonstrating low risk of sudden or subtle incapacitation. Pilots were required to demonstrate good glucose control, including minimal incidence of low glucose levels, to qualify for an SI through this program.

CGM played a large part in risk mitigation for the new ITDM protocol. CGM automatically tracks glucose levels throughout the day and night with readings every 1 to 5 min,[3] and devices are designed to be worn continuously, including during showering, working, exercise, and sleeping. They work though a tiny sensor that is inserted through the skin, often in the abdomen or upper arm, and monitor interstitial glucose levels. These levels are correlated to blood glucose levels. CGM initially required calibration with finger stick levels, ideally at least daily, though the need for such calibration is greatly reduced or eliminated with current generation devices. The sensors can be worn for several days, often up to 10 d, depending on the sensor type. One CGM device is completely implantable and operates for up to 6 mo. The monitor may be part of a pump and/or may be connected to a smart device for monitoring. CGM can also provide patients with smart features such as glucose rate of change, alarms for hypo-/hyperglycemic events, and trends indicating that such events may be imminent. Overall, CGMs have been shown to be effective in improving patient glucose and diabetes control.[2,3] In 2022, the ADA has recommended CGM usage for all adults who take insulin.[24]

The goal of this study was to examine the outcomes of the new ITDM protocol at the FAA. Specifically, this study compares pilots who applied for an SI through the new ITDM protocol and those who were successfully issued an SI to those who were denied.

METHODS

Data Collection

Data was collected retrospectively from the FAA Document Imaging Workflow System (DIWS) for pilots considered for a first- or second-class SI under the ITDM program between November 2019 and October 2021. Inclusion criteria required

submission of information specified under the program (including CGM data) and a final certification decision of SI or final denial (FD). Some pilots applied for a medical certificate upgrade from third-class to first- or second-class; those who were not allowed to upgrade were categorized as an FD.

Once pilots are issued an SI for medical certification, they are required to periodically renew this SI. We collected the number of pilots who applied to renew their SI under the ITDM protocol. We also collected the number of pilots who appealed their initial denial.

For each pilot who met our inclusion criteria, we extracted de-identified data in four major categories: demographics, diabetes parameters, CGM parameters, and diabetic complications. Demographic data included sex and age at application in years. Diabetes parameters included duration of diabetes in years and their most recent hemoglobin A1c (HbA1c). CGM parameters included mean glucose (mg · dl^{-1}), glucose standard deviation (SD), glucose coefficient of variance (CV), time in range (TIR, %), time above range, defined as > 250 mg · dl^{-1} (%), time below range (TBR), defined as < 70–80 mg · dl^{-1} (%), and device wear (%). These parameters were chosen because good control of many of these metrics is shown to correlate with better diabetes control and lower risk of complications. For this study, diabetic complications included the presence or absence of diabetic retinopathy, cardiac complications, neuropathy, and renal complications. Of note, the FAA defines TIR as between 80 mg · dl^{-1} and 180 mg · dl^{-1}; however, not all patients had their devices set to those thresholds, especially early in the protocol. Additionally, settings reflect the clinical recommendations of the pilot's treating endocrinologist specific to the pilot. As a result, the TIR range was not exactly the same for all pilots. Additionally, most low glucose thresholds were defined as < 70 mg · dl^{-1}; however, some devices were set for < 80 mg · dl^{-1}.

Data Analysis

We compared these parameters between pilots issued an SI versus those issued an FD. Age, CGM parameters, and diabetes parameters were analyzed as continuous variables. Continuous variables were analyzed with Mann-Whitney U-test to examine the difference in the median values and distributions for each parameter between pilots who were issued an SI versus those issued an FD. We chose Mann-Whitney U-test as our sample size was not large enough in each group to apply the central limit theorem and many of the variables were not normally distributed. Sex and diabetic complications were considered categorical variables. These parameters were analyzed using a Fisher exact test as sample sizes were small in some groups (e.g., in patients with diabetic complications, **Table I**). All data analysis was done in R.

RESULTS

Of 200 pilots with ITDM identified in the Document Imaging Workflow System (DIWS), 77 met the inclusion criteria. Of these pilots, 55 received SIs and 22 were issued an FD. Demographic details and clinical findings for each pilot are in Table I. Of the 55 pilots who received an SI and were eligible for a continued authorization, 39 were successfully recertificated at the time of the conclusion of data collection. Of those who were denied, three applied for reconsideration, with two ultimately receiving an SI and the third being denied.

Results from the primary analysis are found in Table I. Pilots who received an SI were older (46 vs. 27 yr, $P = 0.002$), had a lower HbA1c (6.50% vs. 7.10%, $P < 0.001$), lower average glucose (139 mg · dl^{-1} vs. 156 mg · dl^{-1}, $P < 0.001$), a lower glucose standard deviation (38 mg · dl^{-1} vs. 53 mg · dl^{-1}, $P < 0.001$), a

Table I. Pilot Characteristics by Final Decision.

PILOT CHARACTERISTICS		FINAL DENIAL (*N* = 22)	SPECIAL ISSUANCE (*N* = 55)	*P*-VALUE
Demographic Data				
Sex (% Male)	*N* (%)	20 (90.9%)	53 (96.4%)	0.574
Age (yr)	Median (IQR)	27.00 (21.2 to 47.5)	46.00 (36.0 to 54.5)	**0.002**
Diabetes Parameters				
Diabetes Duration (years)	Median (IQR)	11.00 (5.0 to 17.0)	9.00 (5.0 to 20.0)	0.667
HbA1c (%)	Median (IQR)	7.10 (6.8 to 7.4)	6.50 (6.0 to 6.7)	**<0.001**
Continuous glucose monitoring (CGM) parameters				
Average Glucose (mg · dl^{-1})	Median (IQR)	156.00 (145.5 to 163.0)	139.00 (128.0 to 149.0)	**<0.001**
Glucose Standard Deviation (mg · dl^{-1})	Median (IQR)	53.00 (45.8 to 61.5)	38.00 (29.5 to 43.5)	**<0.001**
Glucose Coefficient of Variance	Median (IQR)	33.50 (30.2 to 36.6)	26.90 (21.9 to 30.2)	**<0.001**
Time Glucose < 70-80 mg · dl^{-1} (%)	Median (IQR)	2.00 (1.0 to 4.0)	1.00 (0.3 to 2.1)	**0.010**
Time Glucose > 250 mg · dl^{-1} (%)	Median (IQR)	7.60 (2.5 to 11.5)	0.95 (0.0 to 2.0)	**<0.001**
CGM use time (%)	Median (IQR)	91.00 (79.0 to 99.0)	98.00 (95.0 to 100.0)	**0.002**
Time in Range (%)	Median (IQR)	71.00 (61.2 to 80.9)	95.00 (82.0 to 97.0)	**<0.001**
Diabetic Complications (Yes/No)				
Diabetic Retinopathy	*N* (%)	2 (9.1%)	5 (9.1%)	1.000
Cardiac Complications	*N* (%)	0 (0%)	1 (1.8%)	1.000
Neuropathy	*N* (%)	0 (0%)	2 (3.6%)	1.000
Renal Complications	*N* (%)	2 (9.1%)	0 (0%)	0.079

HbA1c: hemoglobin A1c; IQR: interquartile range; CGM: continuous glucose monitoring.

Table II. Median Values for Pilots Receiving a Final Denial and Special Issuance Compared to the 2022 ADA Recommendations.

PARAMETER	ADA RECOMMENDATIONS	FINAL DENIAL PILOTS MEDIAN (IQR)	SPECIAL ISSUANCE PILOTS MEDIAN (IQR)
HbA1c (%)	<7	7.10 (6.8 to 7.4)	6.50 (6.0 to 6.7)
Time in Range (%)	>70	71.00 (61.2 to 80.9)	95.00 (82.0 to 97.0)
Time Glucose < 70–80 mg · dl^{-1} (%)	<4	2.00 (1.0 to 4.0)	1.00 (0.3 to 2.1)
Glucose Coefficient of Variance*	<36	33.50 (30.2 to 36.6)	26.90 (21.9 to 30.2)

ADA: American Diabetes Association; HbA1c: hemoglobin A1c; IQR: interquartile range.
*This metric is mentioned by the ADA; however, it is not part of their recommendations for treatment goal endpoints.

lower CV (26.9 vs. 33.5, $P < 0.001$), and higher CGM use time (98% vs. 91%, $P = 0.002$). Pilots issued an SI also spent less time with low glucose levels (1.0% vs. 2.0%, $P = 0.010$) and high glucose levels (0.95% vs. 7.60%, $P < 0.001$), and spent a higher percent of TIR (95.0% vs. 71.0%, $P < 0.001$). Sex ($P = 0.574$) and duration of diabetes ($P = 0.712$) did not reach statistical significance. There was also no statistical difference in diabetic complications between pilots with an SI and pilots who were denied (Table I).

DISCUSSION

In general, pilots who received an SI for ITDM had better diabetes control than those who were denied. This is especially true when examining CGM parameters and HbA1c. This is not surprising as the FAA criteria for certification of ITDM pilots includes cutoffs for these parameters to ensure that pilots have well-controlled diabetes with a low risk of complications. These cutoff values were based on both ADA recommendations as well as recommendations from FAA endocrine consults.

An HbA1c < 7% has been shown to reduce microvascular complications.[11,12] Currently, the ADA recommendations include an HbA1c < 7% for many nonpregnant adults without a history of significant hypoglycemia (Grade A recommendation). HbA1C levels < 7% are potentially beneficial if they can be achieved safely without significant hypoglycemia or other adverse effects of treatment (Grade B recommendation).[24] TIR has been shown to correlate well with HbA1c, with TIR > 70% corresponding to an HbA1c of approximately 7%.[1] New data also suggests that increased TIR correlates with a decreased risk of complications.[13,24] Tighter control of diabetes additionally reduces the risk of clinical complications.[18] The ADA also recommends a parallel goal of TIR of > 70% with time below range < 4% and time < 54 mg · dl^{-1} < 1% for nonpregnant adults (Grade B recommendation).[24] Time above 250 mg · dl^{-1} demonstrates an increased risk of diabetic ketoacidosis and long-term complications,[14] and the ADA suggests that time above target (glucose > 180) as well as TBR are both useful for re-evaluation of clinical treatment recommendations (Grade C recommendation).[24] Studies also show that hyperglycemia is associated with changes in the central nervous system white matter over time.[5,19]

Another important CGM metric is the SD of glucose levels and the CV that reflects variability relative to the mean (SD/mean). CV is less vulnerable to influence by hyperglycemic excursions than SD. In general, lower variability as represented by a CV of < 33%[16] up to 36%[17] has been considered good clinical glycemic control and hypoglycemic events have been shown to be less prevalent in patients with a CV < 36%.[7,8,17] A high CV (> 36%) was correlated with multiple clinical variables correlating with poor diabetic control such as GFR < 45 ml · min^{-1}, HbA1C > 9%, and a history of hypoglycemia.[7]

Our results show that SI pilots met the ADA's clinical recommendations and the median interquartile range (IQR) values are consistent with clinical and ADA recommendations (**Table II**). This is not surprising, as ADA recommendations were used in creating the certification criteria. However, these results show that the FAA was able to successfully implement a protocol that identified pilots who would be at lower risk for sudden or subtle incapacitation. We also found that denied pilots met (TIR, TBR, CV) or almost met (HbA1c) most ADA criteria (Table II). However, the middle 50% of values (the IQR) for many of the parameters in the denied group often included values outside of the ADA recommendations, demonstrating that at least 25% of denied pilots did not meet ADA criteria for that parameter. Most pilots were denied based on only a few parameters (e.g., they had an acceptable HbA1c, but their TIR or sensor wear time did not meet criteria), which may explain the increased variation of values in denied pilots.

There were no differences in end-organ complications between pilots issued an SI and those who were denied. This is somewhat surprising as there was a large difference in the median time above range [7.60% (IQR: 2.5–11.5%) vs. 0.95% (IQR: 0.0–2.0%)], which generally correlates with diabetic complications.[18] This could be a result of pilots with more severe end-organ damage self-selecting out due to concern of denial or having been denied based on other comorbidities that would preclude certification.

The FAA does not consider age or sex in making certification decisions and duration of diabetes was not one of the parameters used to select pilots eligible for the ITDM. As expected, sex was not significantly different between pilots who received an SI versus those who were denied. The percent of male pilots in this study's population was similar to the percent of male Class 1 and Class 2 pilots (92.4%). Duration of diabetes was also not significantly different between these populations.

Although age at the time of certification is not a factor in decision making by the FAA, there was a statistical difference between the groups. Those pilots who received an SI tended to

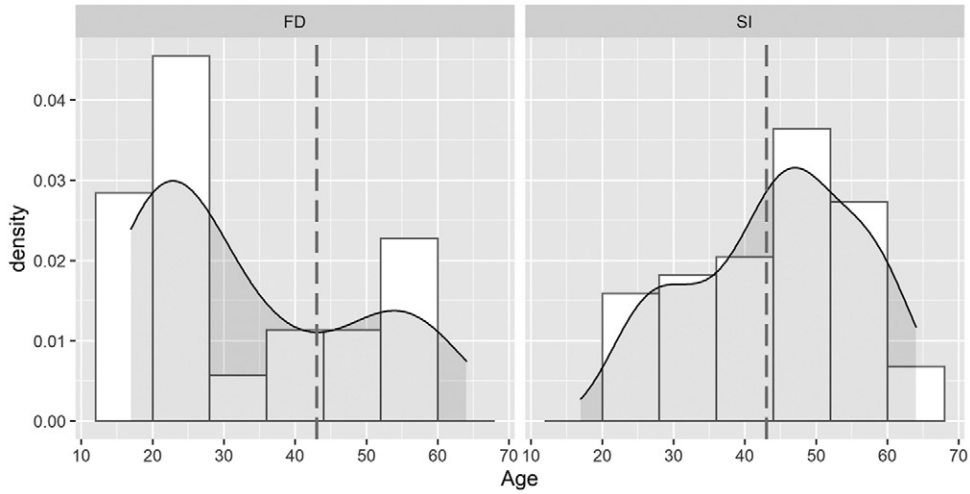

Fig. 1. Distribution of age in years for pilots who received a final denial (FD) and a special issuance (SI).

be older than those who were denied. This was surprising to us as older patients might be expected to have a longer duration of illness and therefore greater likelihood for end organ complications. To this point, duration of diabetes was not statistically significant, which would be consistent with the lack of any significant difference in end-organ disease. All pilots in this study age 22 and under ($N = 7$) were denied, and the distribution of denied pilots was bimodal with a second peak near 50 yr old (**Fig. 1**). One explanation is that younger pilots have more trouble with diabetic control. One study showed that younger patients with type 2 diabetes had worse glycemic control;[22] of note, the two age groups were < 60 and > 60 yr of age and this study was done on a type 2 diabetes population, whereas our population is mostly type 1 diabetics. Another study done in New Zealand found that in patients with type 1 diabetes, HbA1c was highest for the age range between 15–29 yr.[4] Additionally, diabetes is a progressive disease and glucose levels are known to increase with age.[22] This means that older pilots may have fewer hypoglycemic events, the major complication of most concern to the FAA. Additionally, those diagnosed with type 2 diabetes at younger ages may have a severe disease, a higher degree of insulin resistance, and worse glycemic control.[22]

This study is limited by its small sample size and the fact that the data collected for initial certification did not provide sufficient in-flight monitoring data for analysis. In the future, analyzing such data from pilots for the periods in which they are flying may be of interest.

Of note, CGM data measures interstitial blood glucose and is an indirect measurement of blood glucose. This does not appear to be a significant concern as CGM parameters have been highly studied and are reliably correlated to diabetes control. In addition, CGM data is far richer and easily accessible with current technology than traditional finger stick methods. Another concern is that CGM measures interstitial glucose and has a 5-to-10-min lag time when compared to blood glucose measurements. This delay is not important when analyzing retrospective glucose data, but might be critical when CGM is used for real-time decision making by pilots. This is partially mitigated by the generally low prevalence of hypoglycemic events in the certified pilots (as demonstrated by a low TBR) and by the CGMs' ability to analyze trends and notify pilots of "impending" lows so that interventions can be taken before a low occurs.

The FAA created strict standards to mitigate against hypoglycemic events, meaning that some pilots were denied who may eventually be shown to have low risk for incapacitation. This conservative approach is employed to assure the safety of pilots, passengers, and the general public, and to maintain the safety of the National Airspace. As technology for diabetes control improves and clinical guidelines evolve, the ITDM program will continue to adapt. Also, many commercial pilots fly in single pilot operations, and advances in automation has raised interest by scheduled air transport operators (major airlines) to consider transition to single pilot operations as well. The current FAA protocol allows ITDM pilots to perform flight duties without the need for a copilot backup.

The data reviewed also highlight the difficulty the FAA faces in risk-based decision making for ITDM. Clinical providers know that the clinical presentation of patients with ITDM is very diverse. "Acceptable clinical control" differs by the needs and circumstances of the individual patient and may not match generally accepted treatment target ranges. Likewise, no two pilots presenting to the FAA are identical. The FAA's challenge is to distill data comprised of combinations of categorical and almost innumerable continuous values to make a go/no-go decision. Because neither ITDM nor clinical control are static, clinicians look for minimized variability within acceptable targets and overall consistent control consonant with reduced short- and long-term health risks. The FAA takes the same approach a step further to look at the risks during flight. Thus, the FAA go/no-go assessment is not based on any single datum or cutoff values, but an overall assessment of effective clinical control and minimized glycemic variability. The results of this study are consistent with

this, showing that there are significant differences between pilots found eligible for SI and those who are not.

CGM has allowed the FAA to create a program to medically certify pilots with ITDM. This study evaluated the ITDM protocol and demonstrates that the FAA has successfully medically certificated pilots with ITDM for first-/second-class using CGM devices. Pilots granted an ITDM SI reflect significantly better diabetes control, including less time at glucose levels concerning for hypoglycemia. As this program continues and evolves, it will potentially allow many previously disqualified pilots to fly safely.

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