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Identifying and overcoming barriers to diabetes management in the elderly: an intervention study

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14. ABSTRACT
During this research period, we have nearly completed recruitment of patients over age 70 with diabetes and poor glycemic control as defined by A1c>8%, and have started analysis of the data. We have now recruited 50 subjects for the study and have additional data on 16 patients who are in the control arm of the parallel study for better sample size and analysis. We are also performing interim analysis of the results of the cerebral blood flow study. Our baseline data was presented at the annual scientific meeting of the American Diabetes Association last year. This year we have interim data to show effect of interventions. We also have novel data gained by continuous glucose monitoring that will be oral paper presentation at the annual meeting of the American Diabetes Association. The important results show 1) Frequent hypoglycemic episodes were detected by continuous glucose monitoring in older adults even with poor glycemic control. 2) Self-management interventions to overcome barriers to diabetes improved self-care frequency and functionality in older adults 3) different methods of measuring executive dysfunction identifies different deficiencies in older patients with diabetes. Based on our continuous monitoring data, we have received a pilot funding to assess cardiac autonomic dysfunction in older adults with diabetes during continuous glucose monitoring.

15. SUBJECT TERMS
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Introduction:

Subject: Research regarding older adults and, in particular, those with diabetes, lags far behind research on other population segments. Considering the projected increase in elderly patients with diabetes, it is important to study novel but practical strategies to achieve better glycemic control and to improve quality of life in this population.

Purpose: To test whether short-term focused intervention by a geriatric multidisciplinary team with the addition of a geriatric life specialist is superior to usual care (with attention control) in improving glycemic, functional, economic and quality of life parameters in elderly patients with diabetes, and whether these interventions have persistent effects on outcome measures. In addition, the study also evaluates changes in cerebral perfusion in elderly with type 2 diabetes following six months intervention and assess whether changes in cerebral perfusion persist at a one-year follow up.

Scope of the Research: In this study, patients over age 70 with diabetes are randomized to care by either geriatric diabetes intervention team (GDT) or attention control group. Subjects in GDT group undergo comprehensive geriatric assessment and have individualized intervention performed with help of a geriatric life specialist. Intervention by GDT includes focused strategies to overcome barriers in the areas of clinical care, education, social environment, and finances. At the end of 6 months of intervention, the goal is to develop a support network that will empower patients to sustain improvements seen during the intervention. After 6 months of independence period (no contact from GDT), outcome parameters are measured again to see if improvement at 6 months is sustained after 12 months. The subjects in the control group have similar contact time as the GDT group, but with a research team without geriatric expertise. Improvement in clinical, functional, quality of life and economical outcome measures in both groups are compared at 6 and 12 months intervals. At these time points (0, 6 and 12 months) patients are also evaluated for effect of improved glycemic control on cerebral perfusion and glycemic excursions.

Project Tasks:

Task 1: Program Set-up & training and recruitment of study subjects (Mos. 0-36): at Joslin Clinic

During the first year of the study, we received approval from Human Research Protection office (HRPO) at the USAMRMC, for our protocol for compliance with applicable federal, DOD, and Army human subjects protection regulations. Final approval of the whole study protocol including the portion of the study to be performed at the BIDMC was received on 2/8/2008.

During the second year, we have received permission to recruit patients from the Beth Israel Deaconess Medical Center (BIDMC) to increase our recruitment pool. We also received permission to perform continuous glucose monitoring in study subjects to gain insight in to 24 hours glucose patterns and glucose excursions in elderly subjects. We have increased our recruitment efforts and have been able to increase the rate of recruitment.

With additional efforts, we have been successful in recruiting 66.subjects by the end of 36 months (50 subjects for this study and additional 16 subject for parallel study in control group that will be used for analysis).

- Program development, recruitment of geriatric life specialist and training of the geriatric life specialist (Mos. 0-12)

Our program setup was completed in year 1. The study personnel are well trained and are able to follow study protocol effortlessly.

- Identification of study subjects from electronic medical records and recruitment (Mos. 3-36)

We had an excellent system to identify eligible subject from medical records at the Joslin diabetes center. We have called/screened over 200 eligible patients. However, recruitment during winter season in Massachusetts has been difficult. Frequent inclement weather has caused many study visit cancellations in the elderly patients with diabetes, also affecting accrual to the study.

To modify this situation, we submitted our study protocol for approval at the Beth Israel Deaconess Medical Center. We received approval from the human subject protection committee at BIDMC, and submitted the protocol changes to the HPRO at the USAMRMC. Besides adding this center to improve enrollment, we have also encouraged different ways to facilitate transportation in elderly patients. These measures have improved enrollment.

Task 2: Baseline assessment (Mos. 4-36): at Joslin Clinic

- Baseline clinical & survey information collected
- Baseline functional assessment by geriatric diabetes team (GDT) members at the Joslin clinic including nurse practitioner, dietitian and nurse educator.

We have enrolled 50 patients; 34 patients are randomized to the intervention arm and 16 to the attention control arm. We have completed extensive assessments as per protocol and have performed interim analysis on the data. We presented baseline characteristics of the study subjects as abstracts and posters at the American Diabetes Association's annual scientific meeting last year.

Task 3: Team assessment and active intervention by Geriatric care ambassador (geriatric life specialist (GLS) (mos. 4-42) at Joslin Clinic

- Multidisciplinary team meetings to discuss barriers and care plans
- Interventions by GLS and nurse practitioner, including home visits
- GLS performs monthly telephone visits with patients
- Monthly evaluation of care plan by GDT based on GLS tele-visits
- Monthly team meeting to discuss ongoing plan and improvement

Our geriatric lifestyle specialist (GLS) has been well trained and is implementing interventions effortlessly. She continues to work with the GDT and provides the team with a home assessment, performs interventions as directed, and follows up with phone calls to assist in implementing the interventions and strategies uncovered at the assessment and home visit. She provides invaluable feedback to the GDT team members. At the end of the intervention period, she sends plan of care to the study patients to help sustain benefits gained during the intervention period.

Task 4: Outcome parameters assessment and start of independence period (Mos. 10-47):

- Repeat baseline measures on control & intervention groups and assess outcome parameters (mos. 10-41)
- Patients undergo 6 months of independence trial without contact form GDT (mos. 28-47)

20 of our patients have completed intervention period and 8 have also completed independence period.

Task 5: Cerebral vascular studies at baseline, after 6 months of active intervention and 6 months of independence period. (Mos. 3-45) SAFE laboratory at Beth Israel Medical Deaconess Medical Center

- Cerebral perfusion tests including transcarnial Doppler studies, and cerebral vasoreactivity measurement evaluation. SAFE laboratory by Dr. Vera Novak

The subjects, who are randomized to the intervention arm of the study, are scheduled to have a cerebral blood flow study performed at the SAFE lab at BIDMC as per part B of the protocol. All intervention arm subjects have completed this portion of the study at baseline, 12 patients have completed 6 months and 8 have completed 12 months flow studies. Few study subjects declined and some subjects could not complete all the components of the study due to uncomfortable feeling and the study procedure was stopped per protocol. All the other subjects have tolerated the study procedure well.

Task 6: Analysis of data and information distribution. (Mos. 36-48): Joslin Clinic

- Data analysis, conference presentations, preparations for publication

We are now performing interim data analysis. Last year we presented an published baseline data as posters and abstracts at the annual scientific meeting of the American Diabetes Association (ADA). For the purpose of the analysis we have included data from a parallel study assessing older patients with poor glycemic control and combined control group from that study to get better sample size. We have analyzed longitudinal data now evaluating effect of interventions on glycemic control as well as other clinical, functional and psychosocial measures. These data will be presented at the annual meeting of ADA in Orlando, FL from June 25-30, 2010 (attached in appendix).

One important distinction between older vs. younger adults with diabetes is the high prevalence among elderly of co-existing medical conditions and functional disabilities that interfere with self-care [1]. Identifying possible barriers to diabetes self-care is an essential component of developing an effective, individualized diabetes management plans for older adults[2]. Because of the high prevalence of depression, physical disabilities , and cognitive dysfunction among older adults with diabetes, it is imperative that these barriers be identified by specific screenings before formulating a diabetes management strategy. In previous studies, we have shown that subtle, undiagnosed executive dysfunction is an unrecognized co-morbidity among older adults with diabetes and is associated with poor glycemic control[3].

1) Hypoglycemia in older adults

Hypoglycemia is the most important factor limiting efforts to improve glycemic control. However, in the older patient population it is especially dangerous and has poor clinical and functional outcomes [4]. The frequency of hypoglycemia among elderly with inadequate glycemic control remains unknown. We analyze frequency of hypoglycemia from baseline questionnaire in our study patients. All patients were using insulin. Despite poor glycemic control, 42 of 45 (93%) reported episodes of hypoglycemia during the previous 3 months Eighteen of forty-two (43%) reported a hypoglycemia frequency of "more than few episodes a month", while 57% reported "rare episodes". Although typical hypoglycemic symptoms, such as shakiness (56%) and sweating (51%), were frequently reported, atypical symptoms such as weakness (31%),

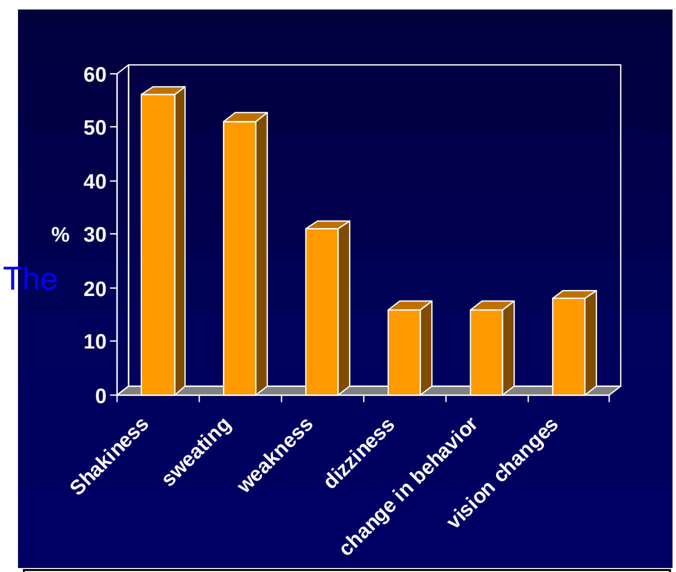

Figure 1: Significant numbers of older adults with diabetes present with atypical hypoglycemia symptoms that can be mistaken for other presentations, e.g. orthostasis, vasovagal episode or worsening of dementia.

change in behavior (16%), dizziness (16%), and vision changes (18%) were also common, and could easily have been missed if not asked for specifically (**Figure 1**). Twenty-four of 60 patients (53%) continued to drive but only 11 (24%) checked their blood glucose before driving. Only 36% with hypoglycemia reported "fear of hypoglycemia". We concluded that hypoglycemia should be carefully looked for among elders, even among those with poor glycemic control.

2) Hypoglycemic and its complications in elderly

Hypoglycemia in older adults is associated with multiple adverse clinical outcomes [5 6 7]. Most feared of these is falls, and fear of falls, leading to decreased functionality and overall quality of life. In certain situations, traumatic falls can lead to institutional placement in older adults. We evaluated the effect of hypoglycemia among our study subjects at baseline. Ninety-three percent of patients reported having hypoglycemia during initial survey. Forty-three percent of patients reported having frequent hypoglycemia ("few times a week" or "few times a month"); 50% of patients had infrequent hypoglycemia ("rare" or "once in a while"), and 7% reported no hypoglycemia. Patients were followed for 3 months after the survey. The results are shown in **Table 1**. The risk of fall increased with increased frequency of hypoglycemia. Fear of falls remained high in all patients, irrespective of hypoglycemia frequency. The risk of emergency room visits and hospitalization increased with increased frequency of hypoglycemia. The A1c (reflecting glycemic control) decreased with increasing hypoglycemia, but remained in the poorly controlled range (A1c >8%). ***Conclusion***: Patients with hypoglycemia are fearful of falling, and have a higher incidence of falls and higher health resource utilization than patients without hypoglycemia.

	No hypoglycemia	Infrequent hypoglycemia (rare, once in a while)	Frequent hypoglycemia (few times a week or month)
Number	4	30	26
Falls	25%	41%	61%
Fear of falls	75%	52%	56%
ER visit	0%	16%	27%
Hospital admit	0%	3%	8%

Table 1: Higher frequency of hypoglycemia is associated with higher incidence of falls, emergency room visits, and hospitalizations

3) Use of continuous glucose monitoring in elderly patients

Continuous glucose monitoring systems (CGMs) are FDA-approved devices that measure interstitial glucose levels at intervals of 1-5 minutes for periods of 3-7 days [8 9]. A sensor with a small filament is inserted and stays under the patient's skin. The sensor is attached to a transmitter that receives glucose readings from the sensor and relays them to a receiver. The receiver is a monitor that receives, and may display, glucose readings from the transmitter (the receiver may also be "blinded" so that patients cannot see the glucose readings). We are using CGM in our patients to identify patterns of glucose excursions and episodes of hypoglycemia. **Figure 2** shows aggregated readings (each color line representing one day) in a representative study patient. As seen in the figure, the patient has significant glucose excursions and multiple hypoglycemic episodes over the 3-day monitoring period. We have performed continuous glucose monitoring in 13 insulin-treated study patients. On an average, the sensor recorded glucose values for 72 hours in all the patients. The range of glucose was 40- 400 mg/dl. Of all glucose values, 56.1 % were >180 mg/dl, and 1.2 % were <70 mg/dl. In this patient group with poorly controlled diabetes, hypoglycemia was not expected. Nevertheless, 7/10 (70%) patients had at least one episode of hypoglycemia (glucose <70 mg/dl) recorded in a 3-day period. The average number of hypoglycemic episodes, among patients with hypoglycemia, was 2.57/3-day monitoring period. By comparison, 4-times-a-day finger-stick glucose measurements, performed during the 3-day CGM monitoring period, detected hypoglycemia in only 2/10 (20%) of subjects. Out of a total of 18 hypoglycemia episodes (glucose <70 mg/dl), 6 episodes occurred during at night (10 pm - 6 am). Pronounced glucose increases and decreases (high and low excursions), as measured by continuous monitoring, occurred frequently in all study subjects and were observed on 36 of 38 CGM monitoring days. A total of 81 high excursions and 13 low excursions were observed. On average, patients experienced 2.1 high excursions and 0.34 low excursions per day. Only 2 patients did not experience any high/low excursions. We concluded that continuous glucose monitoring can be used successfully in older adults. Hypoglycemia can be measured objectively and successfully using CGM and has the added advantage of being able to measure the rate/dynamics of glucose fluctuations (i. e. excursions) as well as identifying nocturnal hypoglycemia episodes.

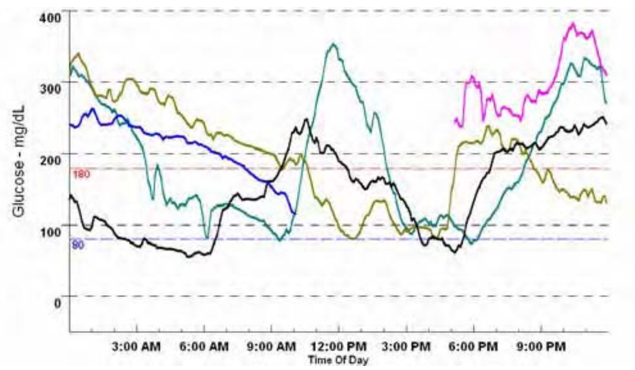

Figure 2: CGM reading in a representative patient showing multiple high and low blood glucose readings

4) Insulin errors in older patients

Co-existing medical conditions, such as cognitive dysfunction and vision/hearing problems, are common in older adults and may interfere with their ability to perform self-care. Insulin injections pose a particularly difficult problem. We evaluated insulin technique in 27 study patients. Twenty-two of 27 (81.4 %) were using insulin. Study participants on insulin were questioned about their insulin use and observed drawing or dialing up their insulin doses. When interviewed, none of the participants reported any trouble taking their insulin. However, when observed by a certified diabetes educator, 12/22 insulin users (54%) with long duration insulin use (average 13.1 years) were found to have difficulty with technique or dosing. Problems with technique included difficulty seeing the lines on the syringe, difficulty with mixing the insulin correctly, difficulty seeing air in the syringe, and inability to follow the insulin injection procedure correctly. Problems with dosing included taking too much or too little insulin, not understanding the insulin regimen, and reports of omitting insulin. The group having trouble with insulin technique and dosing were more likely to miss doses of other medications as well (p =0.009), suggesting problems with medication adherence in general, and were having trouble reading and interpreting food labels (p=0.05), suggesting possible problems with health literacy. Higher frequency of falls, fear of falls, and difficulty walking were more common in the group having problems taking insulin; however, these parameters did not reach statistical significance. There were no differences in glycemic control (A1c 9.5 vs 9.1%), vision problems, cognitive function, depression, or diabetes-related stress in the group having trouble with insulin, compared to the group without difficulty with insulin. We concluded that periodically observing insulin injection technique should be an important part of diabetes assessment in older adults, even among those with a long duration of insulin use. Co-existing medical conditions should be assessed and, where indicated, education regarding insulin injections should be modified to take co-morbidities into account.

5) Effect of exercise capacity in older adults

Exercise is an integral part of diabetes management for all patients but its effect on self-care ability and diabetes related stress in older adults is not well studied. We test exercise capacity in our study subjects using the 6-Minute Walk Test (6MWT). Self-care ability and diabetes-related stress are evaluated using Self-Care Inventory (SCI) and Problem Areas in Diabetes (PAID) questionnaires respectively. Forty-five subjects (age 76±5 years, diabetes duration 22±10 years) were divided into 2 groups based on distance walked during 6MWT at median value (313 meters). Subjects with higher exercise capacity tended to be male (77% vs. 48%, $p<0.05$), Caucasian (91% vs. 50%, $p<0.002$), and had lower BMI (31±6 vs. 35±9, $p<0.04$). This group scored higher on SCI (67±9 vs. 56±14, $p< 0.003$) suggesting better self-care abilities and lower on PAID (18±10 vs. 30±16, $p<0.006$) reflecting less diabetes related stress, compared to subjects with lower exercise capacity. Depressive symptoms (measured by Geriatric Depression scale) were present in 18% of the subjects in the lower exercise capacity group as compared to none in high scoring group ($p<0.03$). Groups did not differ with respect to A1c and measures of cognitive function. However, the higher exercise group had better gait and balance (Tinnetti score 26±2 vs. 22±7, $p<0.004$) and was more likely to be independent in performing activities of daily living (IADL score 16± 0.8 vs. 14±3, $p<0.04$). We concluded that higher exercise capacity is associated with better self-care ability, less depression, less diabetes-related stress and better performance of daily tasks. Exercise education should be stressed in older adults with diabetes to maintain functional independence and optimize quality of life.

6) Effect of social resources in older adults

The effect of the availability of social resources on various aspects in older adults with diabetes in not well studied. We evaluated our study patients for the effect of available social resources on clinical, functional and economic burden. Social resources were assessed by OARS (Older American Resource and Services), a tool developed by the Duke OARS program to assess the availability of physical and emotional resources. A maximum score of 14 reflected excellent availability of social resources. The subjects were divided in to low vs. high resources groups at the mean OARS score of 12. Eighteen of 45 (40%) subjects had a low score on OARS compared to 27/45 (60%) with high score. Age was similar in both groups (76± 6 vs. 76±4 years). Compared to subjects in the high resource group, low social resource group tended to be female (83% vs. 48%, $p<0.01$), had longer duration of diabetes (25 vs. 18 years, $p<0.03$) and lived alone (56% vs. 19%, $p<.009$). In addition, the group with low social resources had higher A1c (9.4±1.2 vs. 8.9±0.5, p<0.05) indicating poor glycemic control, lower exercise capacity as measured by lower score on 6 minutes walk test (235 vs. 364 meters), and higher number of ER visits in past 3 months (44% vs. 15%, p<0.04) suggesting higher healthcare costs, compared to the higher social support group. There was no difference between the 2 groups in the areas of cognitive function, depression, stress related to diabetes management or self-care abilities. We concluded that in older adults with diabetes, inadequate social resources are associated with poor glycemic control, lower functionality and higher health care cost. It is important to assess individual older adults' resources while providing management plans.

Key Research Accomplishments:

1. Research data in older adults with diabetes is scarce. This study fills an important void in information regarding this fast growing population.
2. Research in frail elderly (like the study population – age over 70 years with poorly controlled diabetes) is difficult to conduct. We have successfully recruited older patients and have already gained important insight from baseline data.
3. Interim data from this study shows not only improved glycemic control but also improved functionality in older patients with diabetes who had geriatric specific barriers assessment and interventions.
4. Continuous Glucose Monitoring (CGM) in older adults showed higher than expected prevalence of hypoglycemic episodes. These findings are novel and have resulted in additional funding to assess cardiovascular parameters in older patients during hypoglycemic episodes.

Reportable Outcomes:

Publications 2008-2010:

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2. Alissa R. Segal, PharmD, CDE, **Medha N. Munshi**, MD. Insulin Therapy for Older Adults with Diabetes. In: Geriatrics and Aging. Toronto (Canada): Regional Geriatric Programs of Ontario;2008. p. 357-362.

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4. Elbert S Huang, Priya John, **Medha N Munshi**. Multidisciplinary approach for the treatment of diabetes in the elderly. Aging Health. 2009;5(2):207-216

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7. McMullins D, **Munshi MN**: New ways to look at diabetes in older adults. on the Cutting Edge; Diabetes care and education; 30; 2; 2009

8. **Medha N Munshi**, MD; Elizabeth Blair, MSN, APRN, BC, CDE and Ramachandiran Coopan, MD: Diabetes in Older Adult. Chapter 22; Joslin's Diabetes Deskbook; Editors: Richard S. Beaser, MD and the staff of Joslin Diabetes Center; updated 2nd edition 2010

9. Jesse Foot, MD, Jennifer Giuseffi, MD and Medha N Munshi, MD: Diabetes in the Elderly: Current Cardiovascular Risk Reports. Philadelphia; Current Medicine Group LLC: 2010 (in press)

Abstracts 2008-2009:

1. Emmy Suhl, Laura Desrochers, Patricia Bonsignore, Adrianne Sternthal, Judy Giusti, **Medha N. Munshi**: Higher Exercise Capacity In Older Adults With Diabetes Is Associated With Better Self-Care Ability And Less Diabetes-Related Stress. . In: American Diabetes Association 69th Annual Meeting; New Orleans La; 2009. P. 367-OR
2. Bonsignore P DI, Suhl E, Sternthal A, Giusti J, **Munshi MN**: Unrecognized Errors In Insulin Injection Techniques Are Frequent In Older Adults Even With Longer Duration Of Insulin Use. In: American Diabetes Association 69th Annual Meeting; New Orleans La; 2009. P. 913-P.
3. **Munshi MN**, Iwata I, Suhl E, Giusti J, Bonsignore P, Sternthal A The Risk Of Hypoglycemia Is A Treatment-Limiting Factor In Older Adults Even With Poor Glycemic

Control. . In: American Diabetes Association 69th Annual Meeting; New Orleans La; 2009. P. 2123-Po.

4. **Medha N. Munshi**, Emmy Suhl, Laura Desrochers, Adrianne Sternthal, Judy Giusti, Patricia Bonsignore: Inadequate Social Resources Is Associated With Increased Clinical, Functional And Economic Burden In Older Adults. In: American Diabetes Association 69th Annual Meeting; New Orleans La; 2009. P. 1870-P.
5. Alissa R. Segal, Elizabeth L. Staum, **Medha Munshi**: Polypharmacy Is Associated With Frequent Hypoglycemia, Cognitive Dysfunction, And Poor Nutritional Status In Older Adults With Diabetes. In: American Diabetes Association 69th Annual Meeting; New Orleans La; 2009. P. 562-P.
6. Vera Novak, Peng Zhao, Kun Hu, **Medha Munshi**, David C. Alsop, Jerry D. Cavallerano, Amir M. Abduljalil, Brad Manor, Laura Desrochers, Peter Novak: Relationship Between Inflammatory Markers And Regional Brain Atrophy In Older Diabetics. In: American Diabetes Association 69th Annual Meeting; New Orleans La; 2009. P. 721-P

<u>Abstracts 2009-2010:</u>

1. **Medha N. Munshi**, Emmy Suhl, Adrianne Sternthal, Judy Giusti, Elizabeth Staum, Yishan Lee, Richard Mccartney, Laura Desrochers, Patricia Bonsignore, Alissa Segal. Frequent Hypoglcyemia among Older Adults wit A1c>8% Detected by Continuous Glucose Monitoring. In: American Diabetes Association 70th Annual Meeting; Orlando FL; 2010. P. O123-OR
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4. P. Zao, B Manor, M Munshi, D. Alsop, D. Abduljalil, P Novak, P Roberson, and V Novak. Effects of inflammation on regional vasoreactivity, white matter hyperintensities and brain volumes in type 2 diabetes. In Human Brain Mapping conference 2010

Conclusion:

There is an urgent need to find innovative ways of managing diabetes in elderly patients. We are in a process of identifying variety of barriers faced by this population in performing self-management. We are now getting better at recruiting frail patient population. Our interim analysis of baseline data was well received and appreciated by a large audience at the annual national meeting of the American Diabetes Association. We look forward to finding new and helpful information from our study and plan to distribute the information by presentations at the various meetings and publications.

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Appendices:

1. Frequent hypoglycemia among older adults with A1c>8% detected by continuous glucose monitoring

Burdened with medical and functional co-morbidities, older adults with diabetes struggle to achieve glycemic control, often resulting in increased risk of hypoglycemia. Episodes of hypoglycemia are particularly dangerous in the older population. To reduce the risk of hypoglycemia, relaxation of the standard A1c goal to <8% has been proposed for the frail elderly. However, the effectiveness of this recommendation in reducing hypoglycemia is unknown. We evaluated community-living adults age >_70 years, with A1c>8%, for episodes of hypoglycemia. We used blinded continuous glucose monitoring (CGM) for at least 72 consecutive hours. Patients performed finger-stick monitoring 4 times a day during CGM use and documented symptoms suggestive of hypoglycemia.

CGM was performed on 33 adults for a mean duration of 87.7 hours. Mean age of the population was 75.2 ± 4.6 years, duration of diabetes 18.6 ± 11 years, and A1c 9.4 ± 1.3%. Seventy-seven percent of patients had type 2 diabetes and 91% were using insulin. At least 1 episode of hypoglycemia (glucose <70 mg/dl) per CGM period was observed in 20 patients (61%), with mean glucose level of 61 ± 6.2 mg/dl during the episode. The average number of hypoglycemic episodes was 3.85/patient and average duration was 53 minutes/episode. Eighty percent of patients with hypoglycemia (16/20) suffered at least 1 nocturnal episode (between 10 pm-6 am), with average duration of 52.5 minutes/episode. Out of a total of 77 hypoglycemic episodes, 73 (95%) were unrecognized (not captured by either finger-stick monitoring or by subjective symptoms). All patients with hypoglycemia had at least 1 unrecognized hypoglycemic episode. Only 1/32 nocturnal episodes was recognized by patients. Fifty percent (10/20) of the patients with hypoglycemia had an A1c >9% and 60% (6/10) of these patients had nocturnal hypoglycemic episodes.
Conclusion: Hypoglycemia, especially unrecognized hypoglycemia, is common in older adults, even in those with high A1c levels. This suggests that simply relaxing the standard A1c goal to <8% will not be sufficient to reduce the incidence of hypoglycemia to an acceptable safe level for the frail elderly population with diabetes

2) Self-management interventions to overcome barriers to diabetes care in older adults: A randomized controlled study

Older adults with diabetes face adverse clinical, functional and psychosocial challenges to diabetes self-management. We performed a randomized controlled study to assess whether geriatric-specific intervention strategies can help older adults achieve better glycemic control and improve ability to perform self-care. We randomized adults ≥70 years age with diabetes for ≥1 year, with A1c>8%, to either an intervention or a control group. After baseline assessment of outcome measures, the intervention group had geriatric team evaluation and interventions to optimize their ability to follow diabetes treatment regimen. The attention control group received equivalent time from a separate research staff. Diabetes providers followed all patients for medication management. All patients underwent clinical [A1c, body mass index (BMI)], functional [Instrumental activities of daily living (IADL), and Tinneti Test for gait and balance)], and psychosocial [self-care abilities (Self Care Inventory-revised (SCI)) and diabetes-related distress (Problem Areas in Diabetes (PAID))] assessments at baseline and 6 months.

To date, 58/90 (64%) of the patients (average age 76±5 years, diabetes duration 21±12 years, A1c 9.2 ±1.1%, BMI 33 ±7, 71% type 2, and 93% on insulin therapy) completed 6 months intervention. The most common barriers found were need for diet counseling (88%), medication adjustment (85%) and inadequate exercise (60%). The most common interventions were referral to nutritionist (90%), referral to educator (88%) and earlier appointment with medical provider for medication adjustment (68%). As shown in the table, the intervention arm improved on Tinneti, SCI, PAID, BMI and A1c, while IADL deteriorated in the control arm.

Conclusion: Focused geriatric specific interventions improve diabetes management capability in older adults.

Change from baseline to 6 months	Attention Control N= 18	Intervention N= 40
Tinneti Test*	-2.5±5 (p=NS)	1.3 ±3 (p=0.009)
SCI	1.57±10 (P =NS)	6.9±10.3 (p=0.0002)
PAID	-3.5±10 (p=NS)	-5.6±15 (p=0.03)
BMI	-2.9±8. (P =NS)	-2.3±7(P =0.05)
A1c	-0.37±1.1 (p=NS)	-0.52±1.1 (p=0.005)
IADL	-0.63±0.8 (p=0.007)	-0.08±0.9 (P =NS)

* between-group difference: p=0.0002

3) Different methods of measuring executive function assesses different deficiency in older adults with diabetes

Significant numbers of elderly patients with diabetes have unrecognized subtle cognitive dysfunction, especially executive dysfunction. This condition is not usually obvious at clinic visits and therefore necessitates screening of elderly. Various methods have been used to evaluate executive function. However, their use in older adults with diabetes has not been well studied. Furthermore, the association between executive dysfunction identified with these tests and glycemic control is not well understood.

We performed a cross sectional study on 149 older adults (age≥70 years) with diabetes. Mini Mental State Examination (MMSE) and objective testing of executive functions were performed with a modified clock drawing test (CIB), Trail-making tests (Trail-A and Trail-B), Verbal Fluency (VF), and Hopkins Verbal Learning Test Revised (HVLT-R). Dysexecutive Questionnaire (DEX) was used to measure self-reported executive dysfunction. Demographic and clinical information was collected using questionnaires and surveys including the Geriatric Diabetes Scale (GDS) for depressive symptoms.

We evaluated 149 patients (average age 77±5 years, diabetes duration 16±11 years, mean A1c 7.5±1.2%). Low scores on objective tests, including CIB and MMSE, and high scores on Trail-A and Trail-B tests were associated with poor glycemic control (A1c) ($p<.005$, $p<0.01$, $p<0.01$, $p<008$ respectively). In a multiple regression model, high DEX score was associated with higher diabetes related distress as measured by Problem Areas in Diabetes (PAID) ($p<0003$), depressive symptoms as measured by GDS ($p<0.004$), number of falls in past 6 months ($p<0.03$), fear of falling ($p<0.05$), less years of education ($p<0.001$), and fewer prescription medications ($p<0.002$). Interestingly, the DEX score was not associated with scores on other objective tests of executive function, MMSE or glycemic control (A1c).

Conclusion: In Older adults, executive dysfunction measured only by objective tests is associated with poor glycemic control. Self-reported executive dysfunction is associated with affective symptoms.

4) Received Pilot funding for following grant based on results from current study.

Cardiac Autonomic Dysfunction in Older Adults with Diabetes

Several clinical trials in recent years have shown minimal benefits and, in certain populations, increased risk for poor cardiovascular outcomes with tight glycemic control [10 11 12]. Post-hoc analyses from these clinical trials and from the 10-year follow-up of the UKPDS have suggested that cardiovascular benefits are present in younger and healthier cohorts [13] but not in older individuals and in patients with co-morbidities. Older adults with diabetes are known to have multiple medical co-morbidities. The presence of co-morbidities and possibility of hypoglycemia are thought to be responsible for higher cardiovascular mortality in older adults with tight glycemic control [14]. In addition, patients with diabetes are also at higher risk of cardiac autonomic dysfunction that is associated with increased mortality [15]. In particular, patients with diabetes have increased risk of QT prolongation and reduced fall in nocturnal blood pressure (BP) (i.e. non-dipping) [16, 17]. Patients with diabetes and multiple CVD risk factors are more likely to have prolonged QT interval than those without [18]. Abnormal ventricular repolarizaton resulting from prolongation of QT interval is associated with an increased risk of ventricular arrhythmia and sudden cardiac death and overall excess mortality risk [19]. Furthermore, in young type-1 diabetic subjects, prolonged QT interval is seen during insulin induced as well as spontaneous nocturnal hypoglycemia [20 21]. Additionally, lack of physiological nocturnal fall in BP (non-dipping) is considered a reliable marker of preclinical cardiovascular disease and predictor of future cardiovascular events. Therefore, older adults with diabetes and multiple co-morbidities are at higher risk of QT prolongation, nocturnal non-dipping and ventricular arrhythmias which may be further increased during hypoglycemic episodes. However, frequency and severity of QT prolongation and nocturnal non-dipping in older adults with diabetes, and its association with hypoglycemia remains unknown.

.To address these issues, <u>the over all goal of the proposed study</u> is to evaluate changes in QT interval and BP variability (nocturnal non-dipping) in older adults with and without diabetes with synchronized evaluation by a Continuous Glucose Monitor (CGM) and a Holter Monitor during activities of daily living and during spontaneous hypoglycemic episodes.

This study will provide much needed pilot data to gain insight into the effect of diabetes on parameter of ventricular repolariztioin (QT interval) in older adults. This pilot data will be used to secure further funding to investigate these issues in controlled environment, i.e. lab studies, to understand effect of various levels of glycemia and effect of different classes of drugs on cardiac parameters, autonomic functions and counter-regulatory hormones in older adults.

The <u>importance of this study</u> lies in its potential to help understand the underlying mechanism responsible for the observed lack of beneficial cardiovascular effects of tighter glycemic control in older patients with diabetes. If older adults with diabetes are found to have higher risk of cardiac repolarization abnormalities, it may provide the electrophysiological explanation for increased risk of cardiac arrhythmias and sudden death and may partly explain lack of beneficial effect of tight glycemic control in older adults.

Primary Aim of this study is to examine changes in QT interval in older adults with diabetes compared to age-matched control without diabetes during activities of daily living.

Primary Hypothesis - QT interval will be prolonged in older patients with diabetes compared to non-diabetic controls.

Secondary Aim 1: To examine change in nocturnal BP in older adults with and without diabetes

Secondary Hypothesis 1 – More number of older adults with diabetes will show nocturnal non-dipping compared to non-diabetic controls.

Secondary Aim 2: To examine change in QT interval in older adults during spontaneous hypoglycemic episodes compared to period without hypoglycemia.

Secondary Hypothesis 2 - In older adults with diabetes, those experiencing hypoglycemic episodes (glucose < 70 mg/dl on CGM) will have prolongation in QT interval during the episode compared to non-hypoglycemic period.

This is an innovative study to examine role of ventricular repolarization defect in older patients with diabetes – an unstudied phenomenon.