

Assessing the value of the Ambulatory Glucose Profile in clinical practice

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Abstract

Glycated haemoglobin (HbA_{1c}) is a measure of mean blood glucose levels over time. It is not a good indicator of day-to-day diabetes control and may not reveal variability in blood glucose. Continuous glucose monitoring (CGM) enables the real-time monitoring of glycaemic variability, potentially addressing issues such as episodic hypoglycaemia, hyperglycaemia, and the risk of complications associated with significant glycaemic excursions. Given the quantity of data produced by CGM, there is a need for standardised analysis to enable patterns of blood glucose variation to be revealed. This need has been addressed by the development of specific software – the Ambulatory Glucose Profile (AGP) – which combines inputs from multiple days of CGM data and collates them into a single 24-hour period, making glycaemic patterns more recognisable. In this study, European diabetologists were asked to evaluate the AGP software and report their findings by means of a questionnaire. The results support the use of AGP for analysis of patient glucose data and informing subsequent treatment decisions. When shared with the patient, the AGP results were found to be an effective basis for education, helping achieve better understanding of glycaemic variability and increasing involvement in diabetes self-management.

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Key words: Ambulatory Glucose Profile, glucose variability, glucose monitoring, glucose data, continuous glucose monitoring, hypoglycaemia risk assessment, glycaemic excursions

Introduction

Since the publication of the DCCT, HbA_{1c} has been considered the gold standard for measuring diabetes control,^{1,2} as its correlation with the incidence of microvascular and macrovascular

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Abbreviations and acronyms

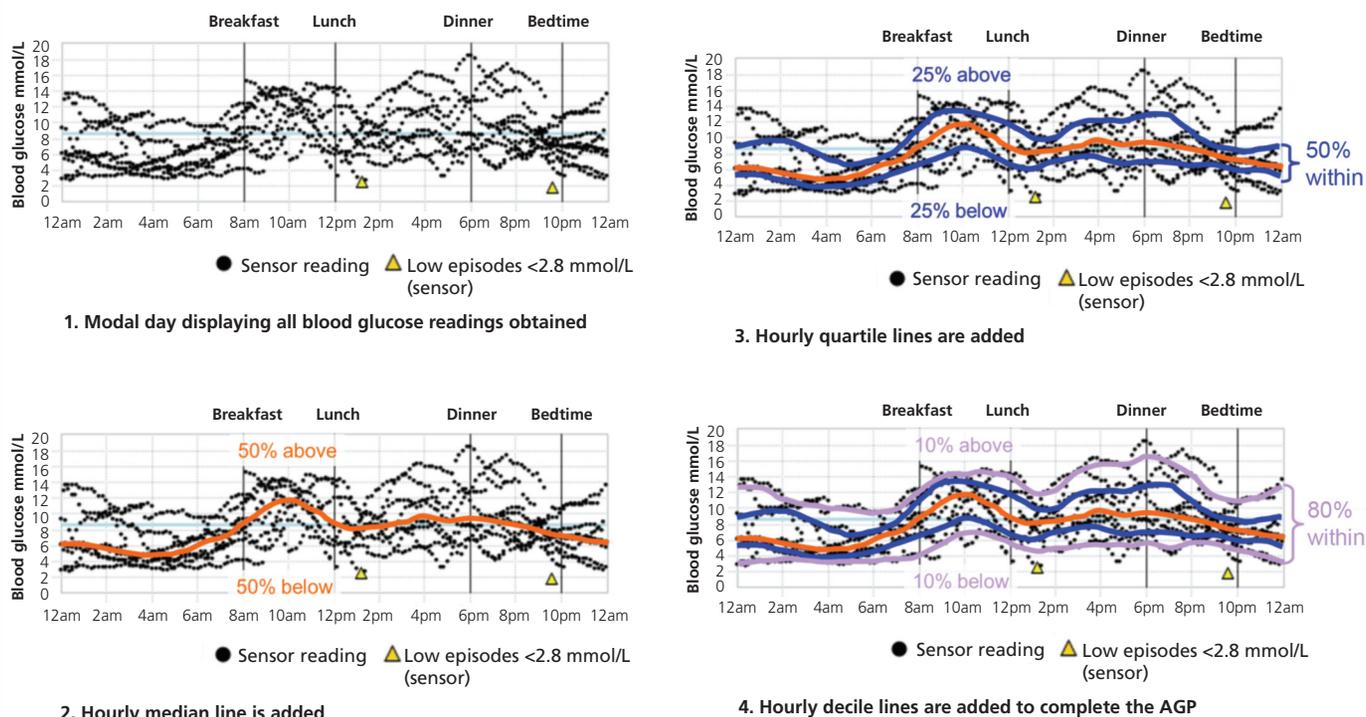
AGP	Ambulatory Glucose Profile
CGM	continuous glucose monitoring
DCCT	Diabetes Control and Complications Trial
FDA	Food and Drug Administration
HbA _{1c}	glycated haemoglobin
IDC	International Diabetes Centre
IQR	interquartile range
SMBG	self-monitoring of blood glucose

complications has been conclusively established in several large, randomised studies.³⁻⁶ Given that red blood cells have a life-span of approximately 120 days, HbA_{1c} is generally considered to reflect mean blood glucose over this period and is therefore not a good indicator of day-to-day diabetes control.¹ This is of particular importance when considering the need to avoid significant extremes of glucose variability and the associated risk of hypoglycaemia or hyperglycaemia.^{1,7,8} There is also evidence that glycaemic variability may have a greater association with the risk of diabetic complications than mean HbA_{1c}. The DCCT study found that, even when HbA_{1c} was comparable, the risk of progression of retinopathy was significantly greater in conventionally treated patients compared with intensively treated patients after 5 to 9 years ($p < 0.01$).^{9,10} One potential explanation for this outcome is the greater frequency and magnitude of glycaemic excursions in conventionally treated patients.⁹ Reducing glucose variability may therefore be an important aspect of effective glucose control.⁹

A significant challenge to effectively understanding glycaemic variability is to find an accurate and standardised method of glucose data collection and analysis.¹ CGM offers the possibility of recording diurnal glucose patterns¹¹ although the data produced by such devices is often unmanageable. There is, therefore, a need for standardised analysis that is easy to understand and which will reveal the important patterns of blood glucose variation. Mazze *et al.*,¹² in collaboration with the IDC, Minneapolis, Minnesota, have produced a software approach called the AGP.¹³ AGP standardises clinical terms and key metrics and presents glucose data visually, making it easy to interpret.

To produce an AGP report, the software combines all CGM data from several days or weeks into a single 24-hour period. The programme then applies mathematical algorithms to help present glycaemic patterns.¹¹ The first component of the AGP to be plotted is the median curve (50th percentile), which shows the median glucose value for every time point and is a representation of glucose stability. The curves immediately above and

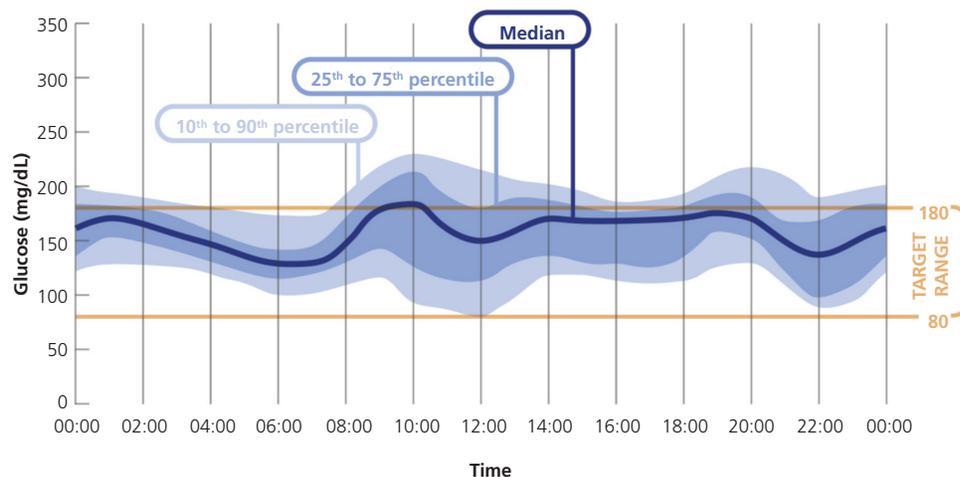
Figure 1. Development of an Ambulatory Glucose Profile (AGP) report, plotting patterns in the blood glucose values displayed in a modal day report



below the median curve define the IQR. The IQR is used to represent glucose variability as it shows the span of 50% of glucose values. The 10th and 90th percentile curves – the two curves on either side of the IQR – track glucose excursions. Thus, when the five curves appear close, there is a fairly high degree of certainty that the variability will be low. By representing the glucose values in this way, the AGP visually and statistically portrays overall diurnal glucose characteristics of glucose exposure, variability and stability, and hence it is possible to rapidly determine whether there is an underlying pattern (Figures 1 and 2).

Bergenstal *et al.* undertook an analysis of the AGP software by asking a panel of US diabetes specialists for feedback on its clinical utility.¹³ Based on their conclusions and recommendations, the

Figure 2. Ambulatory Glucose Profile (AGP) report of 14 days of Continuous Glucose Monitoring (CGM) data, displayed by time to show the spread of glucose values within each time interval. The dark blue line is the median curve (50th percentile) and shows the median glucose value for each time point. The blue shaded area represents the interquartile range (IQR). The outlier values (lowest and highest 10%) are represented by the light blue shaded area.



US FDA announced its support for 'more standardised reporting and analysis of data and information obtained from current glucose monitoring devices.¹⁴ AGP has recently become available for commercial use in Europe and so an expert panel of European diabetologists was set up to further evaluate this approach. The methods and results of this are described here.

Methods

A working group of diabetes specialists from France, Germany, Italy, Spain, and United Kingdom was established. Each specialist was provided with a FreeStyle Navigator II (Abbott Diabetes Care, Alameda, California, USA), consisting of CGM sensor, transmitter and receiver¹⁵ and was asked to analyse data using AGP Software extension to the FreeStyle CoPilot Health Management System software (Abbott Diabetes Care). Patients with type 1 and type 2 diabetes were included. No specific protocol was set and the working group members were asked to:

- Assess AGP in diabetes patients for whom CGM review would normally be indicated
- Assess the benefit of acquiring 14 days of continuous data per patient

A monitoring period of 14 days was selected based on evidence that a minimum of 14 days of CGM is sufficient for identification of glucose patterns¹⁶ and that this period of sensor wear is achievable with the FreeStyle Navigator II.¹⁷

Feedback was gathered via a structured online research questionnaire following 3 months of experience. This research included questions on patient demographics to understand in which clinical situations AGP was examined in, and whether both insulin and non-insulin-treated patients were assessed using the technique. The results were analysed and presented to an expert panel of six diabetes specialists for further consideration.

Results

In the working group 16 diabetes specialists provided data from 59 patients. Of these, 53 patients had type 1 diabetes and the average number of days of data collected per patient was 12.46 (Table 1). Although no protocol was set to dictate specific patient types that should be involved, AGP was mostly used for those who exhibited poor glycaemic regulation and unpredictable glucose excursions. This included patients who had previously experienced unidentified hypoglycaemia or overnight hypoglycaemia, and whose HbA_{1c} did not match with their SMBG values.

The following is a summary of the most informative statistics and responses from the online questionnaire that the working group was asked to complete.

Ease of use and interpretation

Overall, 11/15 of physicians who responded to the questionnaire found AGP easy or very easy to use; 11/15 found the report easy to interpret and 13/15 felt that they could interpret it intuitively, without the need for formal training.

Usefulness in clinical practice

It was agreed by 12/14 respondents that AGP was useful or very

useful in clinical practice and 11/15 agreed that it enabled better understanding of a patient's glycaemic control in comparison with other methods of analysing CGM data. Feedback confirmed that the system enabled the clinician to quickly establish where the main problems in glycaemic control occurred and to consider potential solutions. Of the respondents, 14/15 used the AGP reports in discussion with their patients and, of these, 13/14 agreed that this was useful and served as an educational tool in helping a patient's overall understanding of their diabetes. The respondents considered the role of AGP in patient education as its greatest potential benefit, helping patients better understand their glycaemic control and to become more involved in the management of their diabetes.

Clinical utility of AGP

Respondents identified the main clinical situations where AGP was considered of value as:

- Identifying reasons for a mismatch between the patient's glycaemic profile and HbA_{1c} results
- Assessing a patient's glucose levels versus target range
- Understanding extent and causes of high blood glucose variability
- Assessing suitability of treatment
- Assessing whether it is safe to increase insulin dose

It was suggested that AGP would be less useful for patients who have poor adherence to treatment, or where there is no information available on food and carbohydrate intake, or physical activity. Furthermore, AGP was identified as not being as valuable for patients who are reluctant to make changes to improve their glycaemic control.

A majority (12/15) of respondents agreed that AGP will indicate direction for clinical decision-making on potential changes to the prescribed intervention and 13/15 would recommend its use to other healthcare professionals caring for people with diabetes.

Discussion

The results of this study support previously published evidence that AGP represents a potentially useful tool for analysing individual patient glucose data, and that this approach clearly highlights trends in the variability of a glucose profile, informing subsequent treatment decisions.^{13,18,19} The feedback received in this study suggests a key role for AGP as a tool for patient education.

The responses suggest that AGP enables a better understanding of a patient's glycaemic control in comparison with other methods of CGM data, in particular, the availability of an IQR was considered to be more valuable. It was reported that the evaluation of glucose variability, and hypoglycaemic risk was easier than the Medtronic iPro2 system. However, the insulin dose information available on the Medtronic CareLink Pro was considered to be a benefit that is not present in this version of the AGP report.

As the use of AGP in clinical practice is not yet well reported in the published literature, it remains important to identify in

Table 1 Feedback on the use of the Ambulatory Glucose Profile (AGP) in clinical practice gathered via an online questionnaire. Results are displayed by question type, with the responses for each question given alongside the number of diabetes specialists who answered it

Number of diabetes specialists who responded to the online questionnaire	16/16						
	Total	Type 1 diabetes	Type 2 diabetes				
Patients assessed	59	53 / 59	6 / 59				
	Pump	Basal/bolus	Basal with or without oral	Oral only	Premix		
Type of therapy the patients were prescribed	24/58	29/58	1/58	3/58	1/58		
Average number of days of CGM data included in each AGP report	12.46						
	Very easy	Easy	Neither easy or hard	Hard	Very hard		
Overall, how easy did you find AGP to use?	5/15	6/15	3/15	1/15	0/15		
Overall, how easy did you find the AGP report to interpret?	4/14	7/14	3/14	0/14	0/14		
	Very useful	Useful	Neither useful or not useful	Not useful	Not at all useful		
Overall, how useful did you think AGP was in your clinical practice?	5/14	7/14	2/14	0/14	0/14		
How useful do you think AGP is as a tool to identify any problems with a patient's glycaemic profile and/or the effect of prescribed interventions?	7/15	6/15	1/15	1/15	0/15		
	Yes	No	Not sure				
Do you think that using AGP could contribute to time saving within the clinic, in comparison to using other methods of analysing CGM data?	9/15	1/15	5/15				
When you used AGP for the first time, did you feel that you could interpret it intuitively without the need for formal training?	13/15	1/15	1/15				
In comparison to using other methods of analysing CGM data, would you agree that AGP enables a better understanding of a patient's glycaemic control?	11/15	1/15	3/15				
Do you think that using AGP would give more confidence in making clinical decisions to improve a patient's glycaemic control and/or in changing the interventions for management of a patient?	12/15	1/15	2/15				
Would you recommend using AGP to other healthcare professionals caring for people with diabetes?	13/15	0/15	2/15				
Did you show any of the patients you assessed for this evaluation their AGP report in order to help their understanding of their glycaemic control?	14/15	1/15					
Did you find it useful to show the patients their AGP report as a means of helping them understand their glycaemic control?	13/14	0/14	1/14				
Do you think that AGP could be useful as an educational tool in helping a patient's overall understanding of their diabetes?	14 / 15	0/15	1/15				
	Assessing the patient's blood glucose levels versus target range	Assessing extent and causes of high blood glucose variability	Assessing extent and cause of hypoglycaemia	Assessing suitability of treatment	Assessing whether it is safe to increase insulin	Assessing reasons for a mismatch between the patient's glycaemic profile and their HbA_{1c} results	Other
In which of the following clinical situations do you think AGP has value (please tick all that apply)?	13/15	11/15	10/15	11/15	11/15	13/15	1/15



Key messages

AGP

- combines inputs from multiple days of CGM data and collates them into a single 24-hour period
- is useful for analysis of glycaemic variability, allowing quick identification of poor glycaemic control to inform treatment decisions
- is useful for patient education

which clinical situations AGP may provide most value. It is clear that the patient's treatment regimen, their adherence, and typical food intake must be considered alongside the AGP report. Daily data should also be reviewed as individual hypoglycaemic episodes may be missed. Therefore, the best method of interpreting the report needs to be established, and this has been identified as an area for future investigation.

In conclusion, AGP is a useful tool for clinical practice in Europe. It offers easily interpretable insights to glycaemic variability, which helps healthcare professionals to readily identify areas of concern and suggest possible solutions.

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