Long Term Glycaemic Variability as a Novel Predictor of Graft Patency Following Infra-Inguinal Bypass for Peripheral Arterial Disease

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Background:

Multiple factors influence graft patency following infra-inguinal bypass (IIB). Glycaemic variability (GV), the fluctuations in glycaemia as assessed by standard deviation (SD) of blood glucose or HbA_{1c} measurements, is a novel way of assessing glycaemic control. GV has been associated with increased risk of several adverse outcomes in people with and without diabetes (DM). However, the impact of GV on outcomes following IIB are as yet, undetermined. This retrospective cohort study aimed to assess the impact GV and other known factors on bypass graft patency.

Methods:

A 3-year single centre retrospective case notes analysis of all people undergoing IIB between 2017-2019.
Known predictors of graft patency, mean HbA_{1c} and glycaemic variability (HbA_{1c} variability) were assessed.
HbA_{1c} values for 5 years pre-procedure (with a minimum of 3 measurements) were used to calculate SD of HbA_{1c} (GV).
GV split into quartiles with >9.1 being the worst.

Outcomes:

- Primary patency (PP) – time to re-intervention, ipsilateral amputation or death
- Secondary patency (SP) – time to final graft failure, amputation or death
- Amputation free survival – time until amputation or death

Significant univariate predictors (p<0.10) were entered into multivariate modelling adjusted for diabetes, current smoker status, ischaemic heart disease (IHD), elective vs emergency surgery, Rutherford stage and bypass type

Results:

193 IIB outcomes on 176 patients were analysed on.156 (80.8%) had pre-operative HbA_{1c} for analysis
People with HbA_{1c} >57mmol/mol had longer median hospital stays (p=0.03) and more emergency procedures (p=0.04). Those without diabetes were more likely to smoke (P=0.011), but people with DM had higher Rutherford stage (p=0.0006), underwent more distal bypasses (p=0.004) and more emergency procedures (p=0.04).

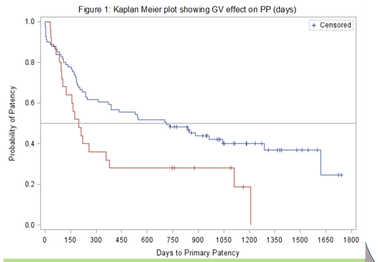
Univariate predictors of graft patency

Variable	Unadjusted HR	95% CI		Pairwise P Value	Estimate P Value
Diabetes	1.45	1.01	2.06	0.042	
HbA_{1c} SD > 9.1 vs < 9.1	1.85	1.09	3.14	0.022	
Rutherford 4 vs 3	2.07	1.24	3.43	0.005	0.011
Bypass type-BK vs AK	2.08	1.26	3.43	0.004	<0.001
Bypass type- Distal vs AK	2.73	1.67	4.46	<0.001	

Multivariate predictors of graft patency

Variable	Adjusted HR	95% CI		Pairwise P Value	Estimated P Value
HbA_{1c} SD 2. > 9.1 vs 1. < 9.1	1.96	1.12	3.42	0.018	
Bypass type BK vs AK	2.54	1.24	5.22	0.011	0.038

GV & Primary Patency



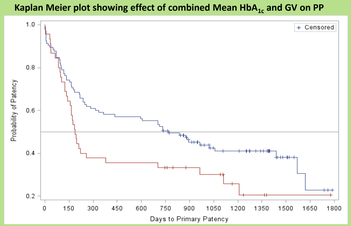
GV >9.1% - 198 [105-377] vs. GV <9.1% - 713 [313-1287] days *(p=0.02)*

GV not associated with:
- SP
- Amputation survivability

Mean HbA_{1c} not associated with:
- PP (p=0.055)
- SP (p=0.170)
- Amputation free survival time (p=0.060)

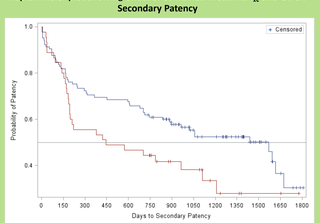
Combined GV & mean HbA_{1c} (mmol/mol)

Kaplan Meier plot showing effect of combined Mean HbA_{1c} and GV on PP



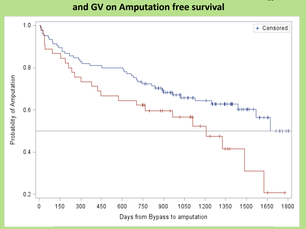
High GV (>9.1%) & HbA_{1c} (>57) -188 [141 to 377]
Vs. Low GV (< 3.2) & HbA_{1c} (<57) - 771 [314 to 1437] days
(p=0.038)

Kaplan Meier plot showing effect of combined Mean HbA_{1c} and GV on Secondary Patency



High GV (>9.1) & HbA_{1c} (>57) - 445 [194 to 1110]
Vs. Low GV (< 3.2) & HbA_{1c} (<57) - 1570 [835 to 1674] days
(p=0.043)

Kaplan Meier plot showing effect of combined Mean HbA_{1c} and GV on Amputation free survival



High GV (>9.1) & HbA_{1c} (>57)
Vs. Low GV (< 3.2) & HbA_{1c} (<57)
(p=0.037)

Discussion:

This is the first study to assess the impact of long term GV on post-operative outcomes following IIB.
GV has been shown to be a independent predictor of graft patency even after multivariate adjustment, when diabetes status and mean HbA_{1c} are no longer significant. This suggests that GV could be a more important predictor than diabetes status and mean HbA_{1c}.
Furthermore, mean HbA_{1c} was only associated with PP, SP and amputation survivability when combined with GV. Therefore, GV should be an additional measure of glycaemic control and a additional therapeutic target to improve post-operative outcomes.
GV could be more important than mean HbA_{1c} in predicting graft failure and therefore more significant in operative risk reduction.
This research argues that we should be aiming for both a Low HbA_{1c} and HbA_{1c} consistency before and after surgery.
Therefore, GV could have a wide range of clinical applications within surgery.

Conclusion:

We have demonstrated GV and level of bypass to be independent predictors of graft failure on multivariate analysis. Patients with greater GV had a nearly 2-fold increase in risk of graft failure. Therefore, optimising GV, particularly for elective bypass, could be an additional therapeutic target, where possible, to improve post-operative outcomes.

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